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المملكة العربية السعودية

وزارة التعليم العالي

جامعة أم القرى

كلية العلوم التطبيقية

قسم الكيمياء

٥٥٤٠



٣٠١٠٢٠٠٠٠٠٤٧٦٧

اصطناع وتطبيق لبعض مشتقات الكينولين الحلقية

غير المتجانسة الجديدة

رسالة مقدمه إلى قسم الكيمياء - كلية العلوم التطبيقية

جامعة أم القرى بمكة المكرمة

من

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تحت إشراف

الأستاذ الدكتور / علي أحمد محمد الحافظ

أستاذ الكيمياء العضوية - قسم الكيمياء

كلية العلوم التطبيقية

جامعة أم القرى بمكة المكرمة

المملكة العربية السعودية

١٤٢٤هـ / ٢٠٠٤م



لِكُلِّ دَرَجَةٍ مِّمَّا عَمِلُوا وَمَا رُبُّكَ بِغَافِلٍ عَمَّا
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Kingdom Of Saudi Arabia
Ministry Of Higher Education
Umm AL-Qura University
Faculty Of Applide Science
Chemistry Department

SYNTHESIS AND APPLICATION OF SOME NEW HETEROCYCLIC QUINOLINE DERIVATIVES

Thesis

Presented to the Chemistry Department, Faculty of Applied Science,
Umm-Al-Qura University, Makkah, Saudi Arabia

For the Degree of Doctor of philosophy of Science,
Ph.D. (Organic Chemistry)

Presented by

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3-	Advanced Physical Chemistry	95/100

Second Semester (1421 AH.): (6 hours/week)

1-	Inorganic Chemistry	97/100
2-	Advanced Organic Spectroscopy	93/100
3-	Selected Topics in Organic Chemistry	<u>100/100</u>
Total		582/600

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Finally as a mark of respect and gratefulness, I affectionately thank my parents, sisters and brothers for their love support and for having given me an opportunity to pursue higher studies.

Nariman M.A. Nahas

Contents

	Page
Summary	i
Aim of Work	ii
Introduction	1
Results & Discussion	34
Experimental	51
List of New Compounds	84
References	86
Appendix	97
Arabic Summary	

Summary

SUMMARY

The work presented in this thesis involves the synthesis and reactions of a variety of tri-, tetra- and pentacyclic heterocyclic quinoline derivatives of potential biological interest.

The pyrano[3,2-h]quinoline derivatives **218_{a-e}**-**219_{a-e}** were used as starting materials in our synthetic studies and were used as key intermediate in the synthesis of fused heterocyclic systems. Thus the pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**220_{a-e}**-**222_{a-e}**) were produced when compounds **218_{a-e}** were reacted with acetic anhydride/pyridine mixture, formamide and formamide/formic acid mixture respectively.

4-Aryl-3-cyano-6-chloro-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]quinolines (**223_{a-e}**) were obtained by refluxing compounds **218_{a-e}** with triethyl orthoformate; these compounds **223_{a-e}** underwent aminolysis and cyclization by treatment with aniline to give the corresponding derivatives **224_{a-e}**. Interaction of **218_{a-e}** with ethyl cyanoacetate led to the formation of pyridopyranoquinolines **225_{a-e}**. However, compounds **218_{a-e}** gave the corresponding triazine derivatives **226_{a-e}** by means of diazotization with sodium nitrite in AcOH/HCl mixture.

Imidazopyranoquinolines **227_{a-e}** could be obtained by the reaction of compounds **218_{a-e}** with ethylenediamine. Cyclization of compounds **227_{a-e}** with triethyl orthoformate, aldehydes and ketones gave the corresponding derivatives **228_{a-e}**-**230_{a-e}**, respectively. While, the reaction with cyclic ketones and carbon disulfide gave the spiro and thioxo derivatives **231_{a-e}**-**233_{a-e}** respectively.

Moreover, interaction of compounds **218_{a-e}** with nitrous acid gave the dichloro derivatives **226_{a-e}** which in turn, proved to be a useful intermediate. Compounds **235_{a-e}**-**236_{a-e}** were produced from the reaction of **234_{a-e}** with formic acid and carbon disulfide respectively. In addition, treatment of **234_{a-e}** with acetic acid and sodium nitrite solution at rt gave the azido derivatives **237_{a-e}**.

On the other hand, the amino function of compounds **219_{a-e}** were easily converted to the corresponding 1-pyrrolyl group via the interaction with 2,5-dimethoxytetrahydrofuran in boiling acetic acid to give the pyrrolyl ester **238_{a-e}** which reacted with hydrazine hydrate to give the pyrrolyl hydrazide **239_{a-e}**. The latter compounds **239_{a-e}** were used for the synthesis of the pyrazolyl and acid azide derivatives **240_{a-e}**-**241_{a-e}** by reaction with acetylacetone and nitrous acid respectively.

The acid azide is a versatile compound and could be transformed into a variety of derivatives. When compounds **241_{a-e}** were heated in boiling ethanol, the ethylcarbamates **242_{a-e}** were obtained. When they reacted with hydrazine hydrate gave the semicarbazides **243_{a-e}**. Heating the acid azide in a high boiling point solvent such as xylene led to Curtius rearrangement with concomitant ring closure of the isocyanate intermediate **241_{a-e}** giving pyrrolopyrazinopyranoquinolines **244_{a-e}** which could be transformed into the corresponding chloro derivatives **245_{a-e}** when heated with phosphoryl chloride.

The reactivity of the chlorine atom at C-9 of **245_{a-e}** was shown by its easy displacement using various nucleophilic reagents such as hydrazine hydrate to give the hydrazino derivatives **246_{a-e}**. Finally, the triazolo derivatives **247_{a-e}** and **248_{a-e}** were produced from the reaction of **246_{a-e}** with acetic acid and carbon disulfide, respectively.

Some of the newly synthesized compounds were selected for testing of their biological activity, such as antibacterial and antifungal activity. The preliminary results are herein reported.

AIM OF WORK

Heterocyclic chemistry represents one of the major sources for supplying drugs, dyes and chemical industries with new materials. Several correlations have been reported between structure and biological activity is expected to increase biological activity or to develop new ones.

Interestingly, the main target of the presented work is to synthesize some new heterocycles containing pyranoquinoline fused with pyrimidine, triazine, imidazole, pyridine, triazolopyrimidine, pyrrole, pyrrolopyrazine and triazolopyrrolotriazine moieties in an endeavor to develop new materials of anticipated strong biological activities.

Introduction

INTRODUCTION

Heterocyclic compounds are encountered in a very large number of groups of organic compounds. They play a vital role in the metabolism of all living cells, which are widely distributed in nature and are essential to life. Mechanistic investigations enhanced the general understanding of these compounds. Heterocyclic compounds have interesting theoretical implications, diversity of synthetic procedures and physiological and industrial significance. Pyrimidine and purine bases of the genetic material DNA, the essential amino acids, proline, histidine, tryptophan and the oxygen transporting pigment haemoglobin are some of the important biomolecules which incorporate nitrogen heterocyclic systems in their structures. Also, a large number of nitrogen heterocyclic compounds find varied applications as dyestuffs, plant-growth regulators, agrochemicals, herbicides, reductive antibacterial and antitumour agents.

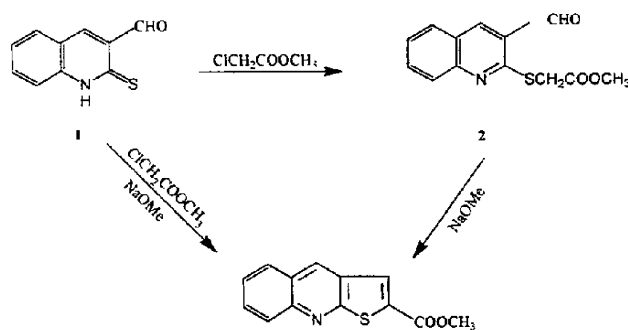
In connection with the search for newer physiologically active compounds, several reports have appeared on the synthesis of fused heterocyclic quinoline derivatives which were found to be useful as: antipsychotics,^{1,2} antiasthmatics,³ antibacterial,⁴⁻⁷ antihypertensive agents,⁸ anticoccidials-1,⁹ antiplatelet agent,¹⁰ antimalarials,¹¹ antiulcer,¹² antidiabetic agents,¹³ anti-(tumor, atherosclerosis, psoriasis, diabetes and arthritis activities),¹⁴ fungicides,¹⁵⁻¹⁷ herbicides,¹⁸ lipoxygenase inhibitors,¹⁹ inhibitors of MEK enzymes,²⁰ immunostimulants²¹ and immunosuppressants,²² inhibitors of methionyl t RNA synthase,²³ dopamine D₄ receptor ligands,²⁴ gonadotropin releasing hormone antagonists,²⁵ phosphodiesterase IV (PDE) inhibitors,²⁶ potassium channel openers,²⁷ PDGF(platelet derived growth factor) receptor and / or LCK tyrosine kinase inhibitors,²⁸ epidermal growth factor receptor signal transduction inhibitors,²⁹ cardiovascular activities,³⁰ steroid receptor modulators,³¹ NK-3 and NK-2 receptor antagonists,³² effective in the therapy of irritable bowel syndrome,³³ for treating urinary incontinence³⁴ and inhibitors of steel corrosion in acid media.³⁵ On the other hand, pyran derivatives exhibit antimicrobial activities,^{36,37} antitumor,³⁸ anticholesterolemics and platelet aggregation inhibitors,³⁹ growth stimulating effects,⁴⁰ as immunomodulators,⁴¹ cyclooxygenase-2-inhibitor,⁴² leukotriene B₄ (LTB₄) antagonists,⁴³ hypotensive effect,⁴⁴ central nervous system activity,⁴⁵ in treating neurological disorders⁴⁶ and hypersensitive ailments⁴⁷ and in the prevention and treatment of gastrointestinal diseases.⁴⁸ Moreover, fused pyrimidines

were found to possess a wide biological activities as antimicrobial,^{49,50} antiparkinsonian,⁵¹ anticancer,⁵² antiviral,⁵³ herbicides,⁵⁴ leishmanicidal,⁵⁵ insecticidal,⁵⁶ kinase inhibitors⁵⁷⁻⁶⁰ and as potential antimycotic agents.⁶¹ Also, a wide range of biological activities has been attributed to fused imidazole and triazines, for instance imidazoles are used as antihypertensive,⁶² antiallergic,⁶³ antibacterial,⁶⁴ protein kinase C inhibitors,⁶⁵ antidiabetes,⁶⁶ carcinogens,⁶⁷ analgesic activity,⁶⁸ thrombin receptors,⁶⁹ vascular damaging agents,⁷⁰ GAB A_a receptor complex modiators,⁷¹ insulin resistant improvement agents,⁷² immune response modifiers,⁷³ H3-histamine receptor antagonists,⁷⁴ human growth hormone mimetics⁷⁵ and proton pump inhibitors.⁷⁶ Triazoles and triazines are used as antipsychotic agents,⁷⁷ fungicides,⁷⁸ antimicrobial,^{79,80} herbicides,⁸¹ blood platelet anti-aggregation⁸² and cardiotonic agents.⁸³

Based on these findings, it was of interest to introduce these biologically active moieties in one molecule, giving rise to a new series of potential biochemically active compounds. Therefore many references are dealing with the synthesis and applications of fused heterocyclic quinoline derivatives which are enough to be collected in several texts. From this point of view, we will restrict the introduction of this thesis on the recently, closely and highly related references to our interest as thienoquinolines, pyrimidothienoquinolines, pyrazoloquinolines, pyranoquinolines, pyrroloquinolines and triazolopyrimidoquinolines.

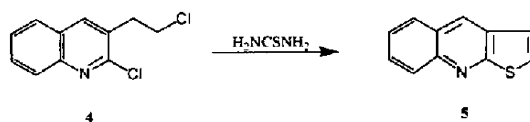
Preparation of some selected fused heterocyclic quinolines:

The reaction of formylquinoline thione⁸⁴ (1) with a slightly excess of chloroacetic acid ester gave the corresponding ester (2) which undergoes ring closure with sodium methoxide to thieno[2,3-b]quinoline (3) (Scheme 1).



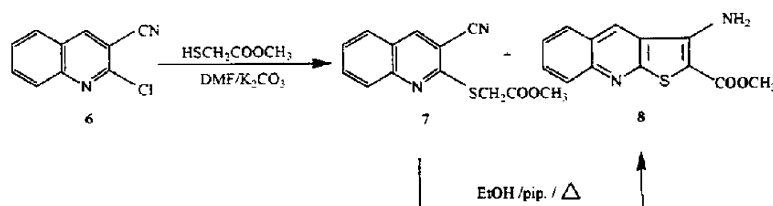
Scheme 1

It was found that⁸⁵⁻⁸⁷ the reaction of the chloroethylquinoline (**4**) with thiourea in refluxing ethanol gave the thieno[2,3-b]quinoline (**5**) in good yield (Scheme 2).



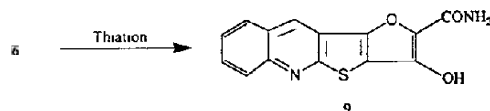
Scheme 2

Neelima *et al*⁸⁸ mentioned that the reaction of 2-chloro-3-cyanoquinoline(**6**) with $\text{HSCH}_2\text{COOCH}_3$ gave a mixture of methyl[3-cyano-2-quinoliny]thio]acetate(**7**) in low yield and methyl-3-aminothieno[2,3-b]quinoline-2-carboxylate (**8**) in a good yield (Scheme 3).



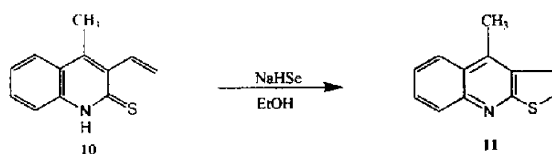
Scheme 3

Also, compound (**6**) was converted into furothienoquinoline⁸⁹ (**9**) by thiation, followed by two cyclocondensation reaction with ClCH_2CN (Scheme 4).



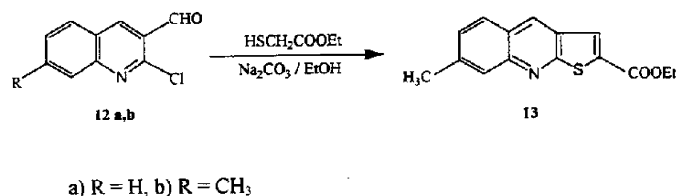
Scheme 4

Raja⁹⁰ reported that upon refluxing of vinylquinolinethiones (**10**) with sodium hydroselenide in EtOH gave thieno[2,3-b]quinoline (**11**) (Scheme 5).



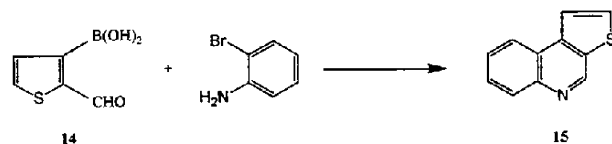
Scheme 5

Recently⁹¹, the reaction of 2-chloro-3-formyl-7-methylquinoline (**12_b) with HSCH₂COOEt in EtOH containing anhydrous Na₂CO₃ gave 2-ethoxycarbonyl-7-methylthieno[2,3-*b*]quinoline (**13**) (Scheme 6).**



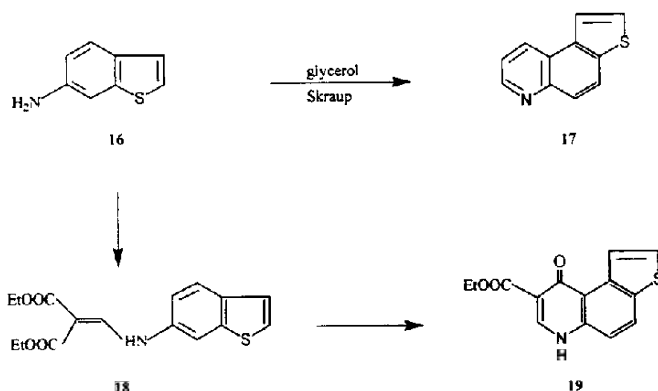
Scheme 6

The thieno[2,3-*c*]quinoline⁹² (**15**) was prepared by reacting 2-formyl-3-thiopheneboronic acid (**14**) with 2-bromoaniline in the presence of (Ph₃P)₄Pd as a catalyst in basic medium (Scheme 7).



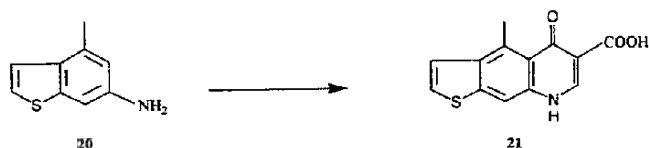
Scheme 7

Sauter *et al*⁹³ found that the application of Skraup reaction to 6-aminobenzo[*b*]-thiophene led to the formation of the thieno[3,2-*f*]quinoline (**17**). However, the reaction of (**16**) with ethoxymethylene diethylmalonate gave compound **18**, which was cyclized via Gould-Jacobs reaction to give thieno[3,2-*f*]quinoline derivative (**19**) (Scheme 8).



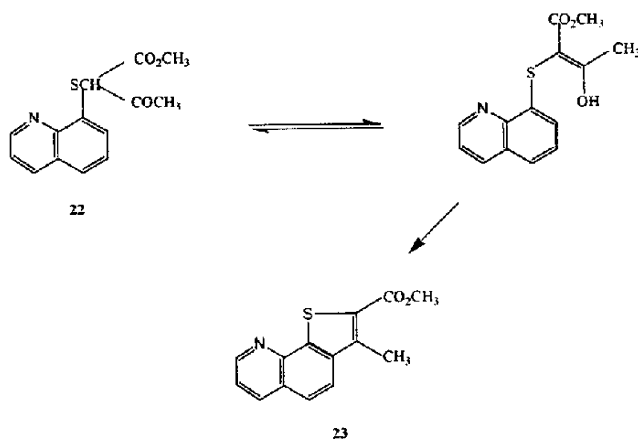
Scheme 8

The cyclization⁹⁴ of benzothiophenes (**20**) with $\text{EtOCH}:\text{C}(\text{CO}_2\text{Et})_2$ followed by ester hydrolysis gave the thieno[3,2-g]quinoline(**21**) (Scheme 9).



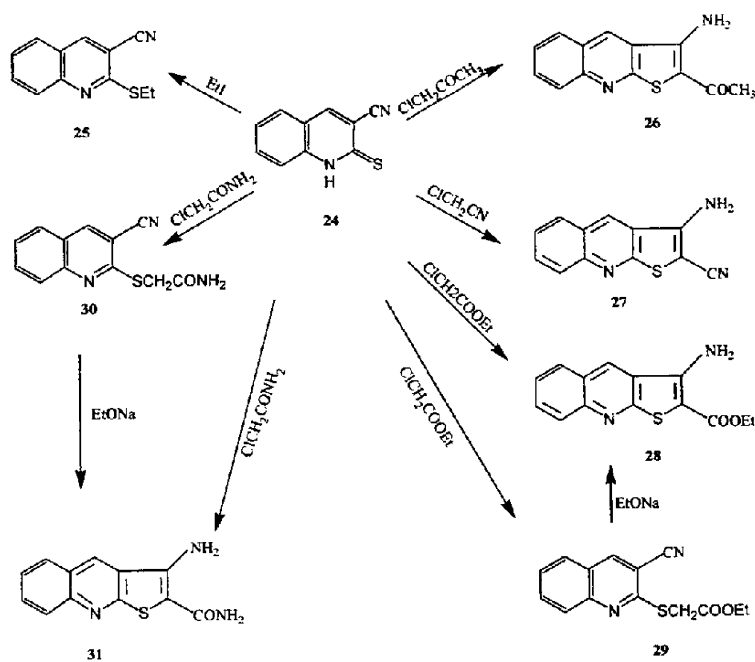
Scheme 9

Sasaki *et al*⁹⁵ reported that the thioquinoline derivative **22** underwent photocyclization via its enolic form to give **23** (Scheme 10).



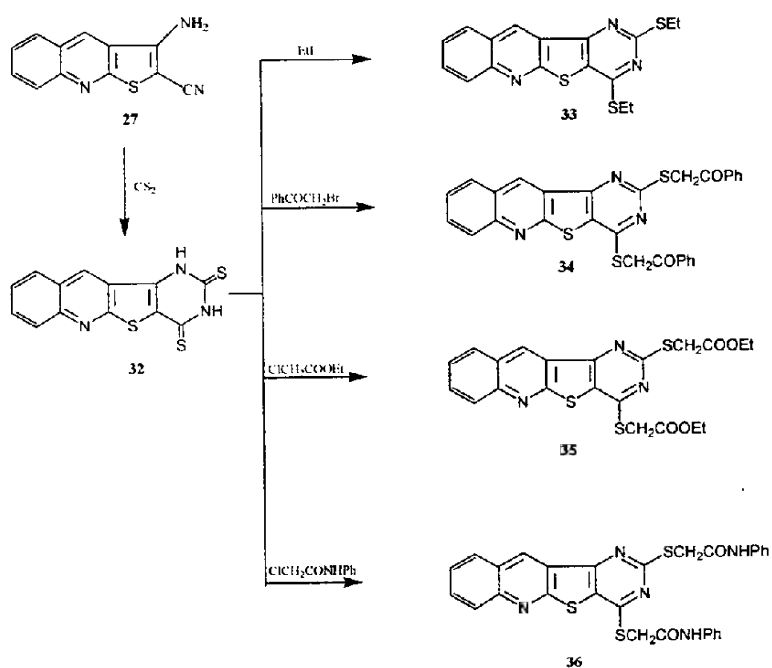
Scheme 10

Recently⁹⁶ it was reported that 3-cyanoquinoline-2(1H)thione (**24**) was reacted with some halo compounds to give S-substituted thioquinoline derivatives **25,29** and **30**. Cyclization of **30** yielded thienoquinoline **31**. Also, reaction of **24** with chloroacetone, chloroacetonitrile, ethyl chloroacetate and chloroacetamide furnished thienoquinolines **26,27,28** and **31** respectively (Scheme 11).

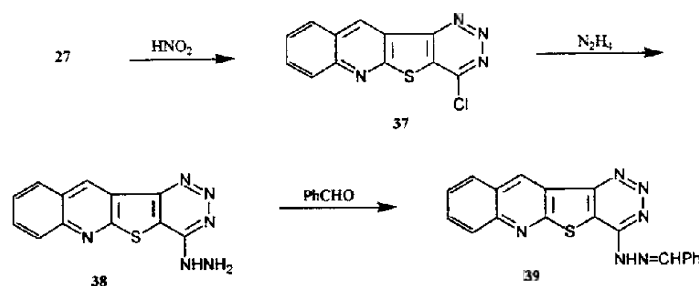


Scheme 11

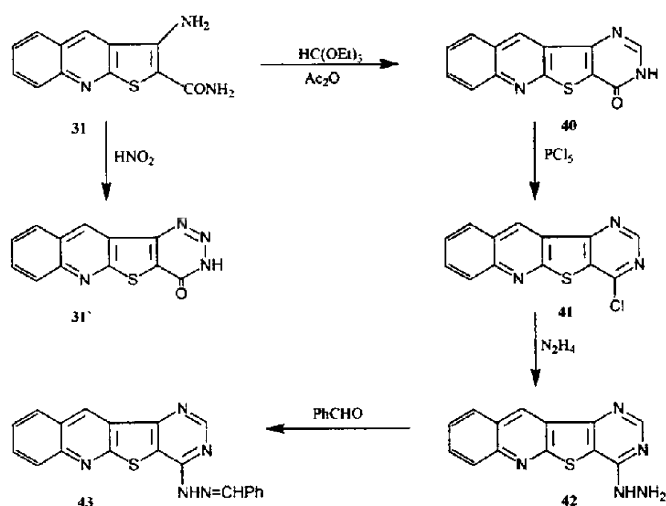
Moreover, compound 27 and 31 underwent different sequence reaction to give some new pyrimido-and triazino[4',5':4,5]thieno[2,3-b]quinoline derivatives (32-44) (Scheme 12-14).



Scheme 12

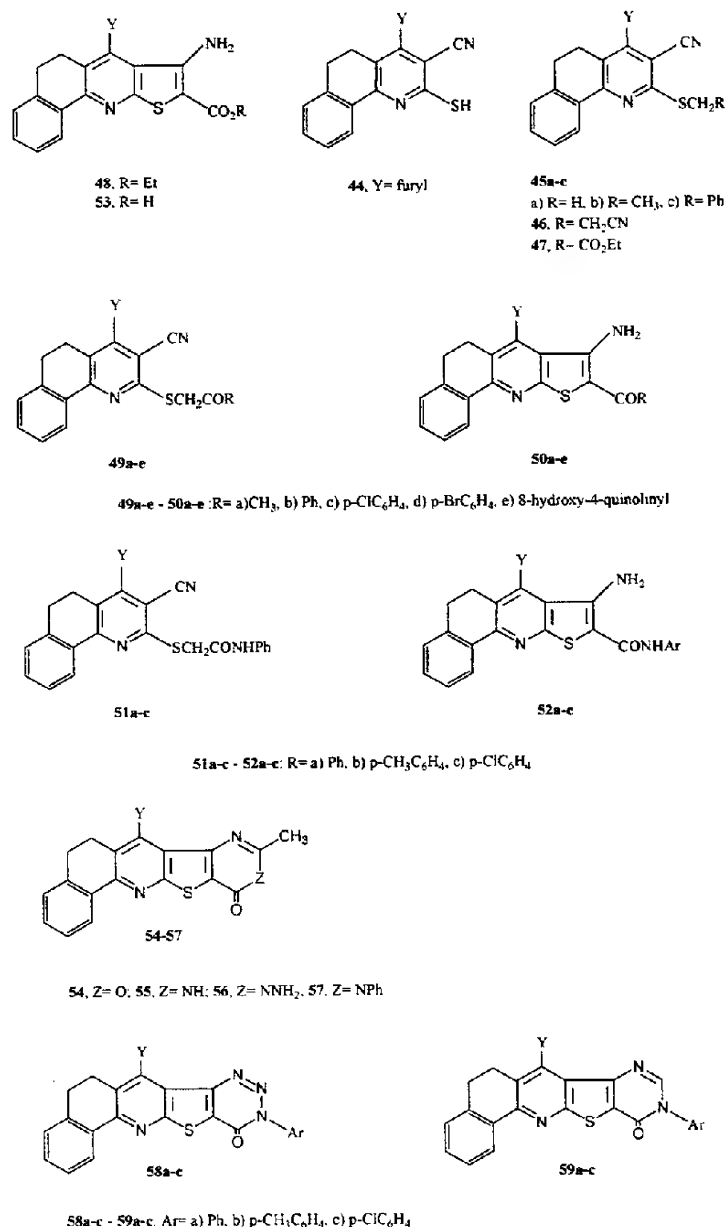


Scheme 13

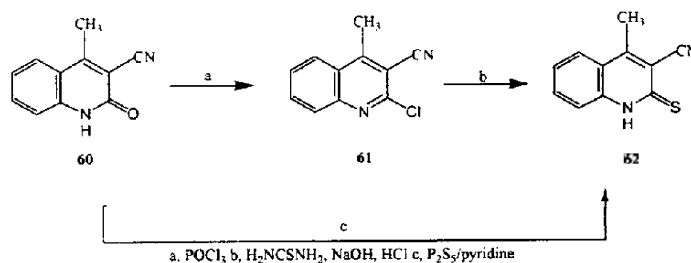


Scheme 14

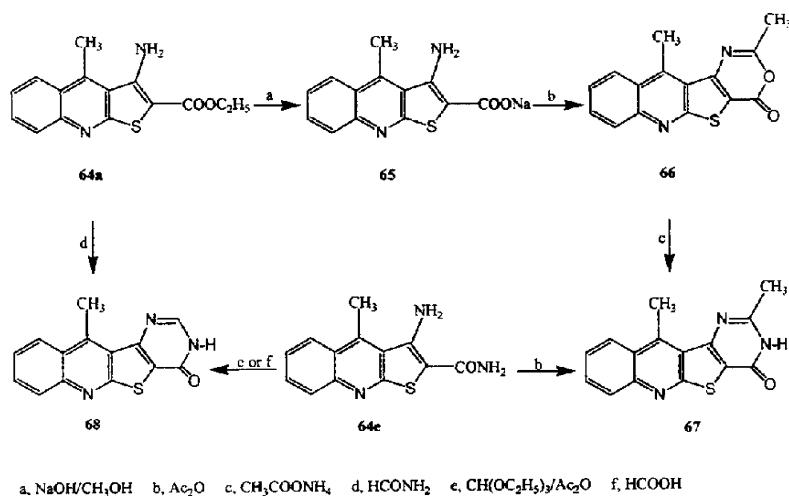
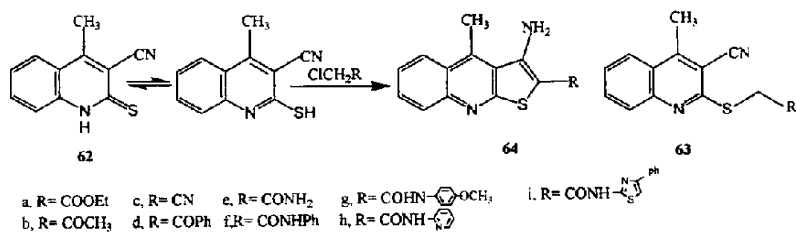
Bakhite⁹⁷ mentioned that a series of new 3-cyano-5,6-dihydro-4-(2-furyl)-2-(substituted)thio-benzo[h]quinolines (**45_{a-c}**, **46**, **47**, **49_{a-e}** and **51_{a-e}**) have been prepared from 3-cyano-5,6-dihydro-4-(2-furyl)benzo[h]quinoline-2(1H)thione (**44**). Compounds **47**, **49_{a-e}** and **51_{a-c}** on treatment with appropriate base underwent smooth cyclization into thieno[2,3-b]benzo[h]quinolines (**48**, **50_{a-e}** and **52_{a-c}**), respectively. Hydrolysis of ester **48** gave the corresponding acid **53** which was converted to oxazinone **54** by heating in acetic anhydride. Oxazinone **54** in turn, was recycled into pyrimidinone derivatives **55-57** upon treatment with ammonium acetate, hydrazine hydrate and aniline, respectively. Compound **52_{a-c}** were reacted with nitrous acid and with orthoformate to produce the fused polycyclic quinoline derivatives **58_{a-c}** – **59_{a-c}**.



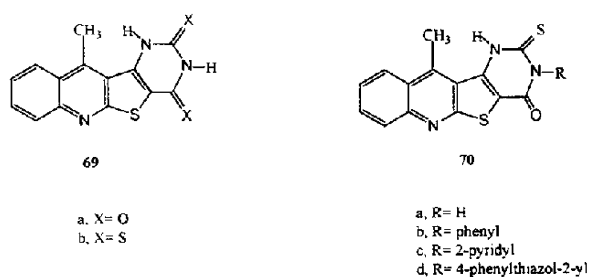
El-Kashef *et al*⁹⁸ reported the synthesis of oxazino[4',5':4,5]thieno[2,3-b]quinoline (**66**), pyrimido[4',5':4,5]thieno[2,3-b]quinolines (**67-70**), triazino[4',5':4,5]thieno[2,3-b]quinolines (**71**) and imidazo[4',5':4,5]thieno[2,3-b]quinolines (**75**) (Schemes 15-21).



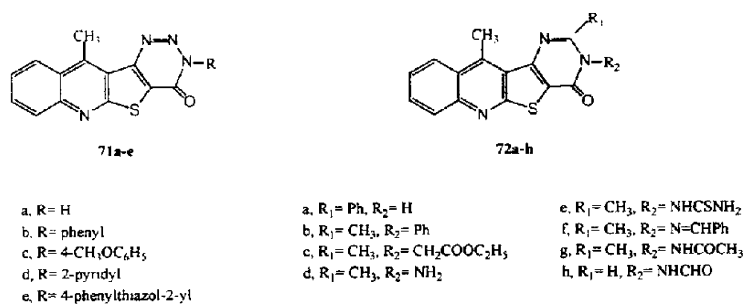
Scheme 15



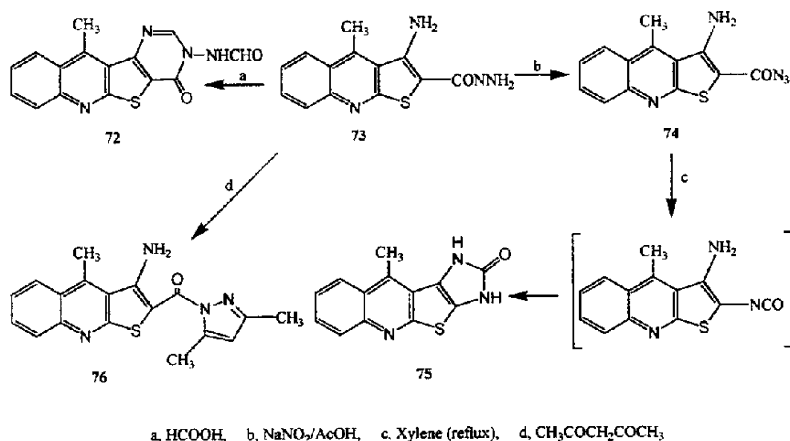
Scheme 16



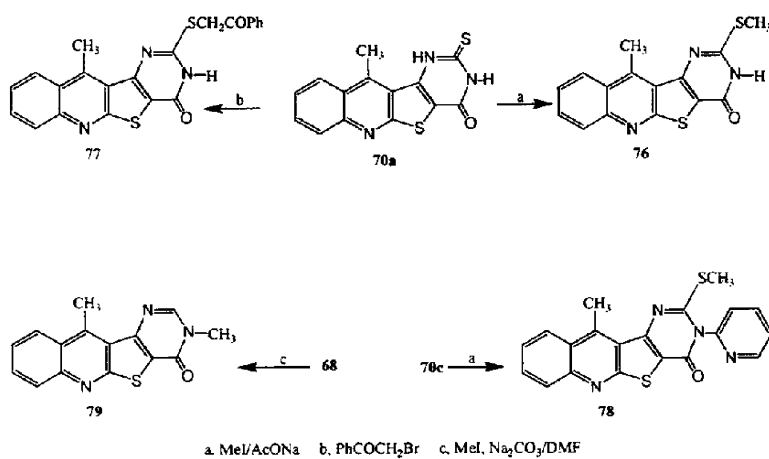
Scheme 17



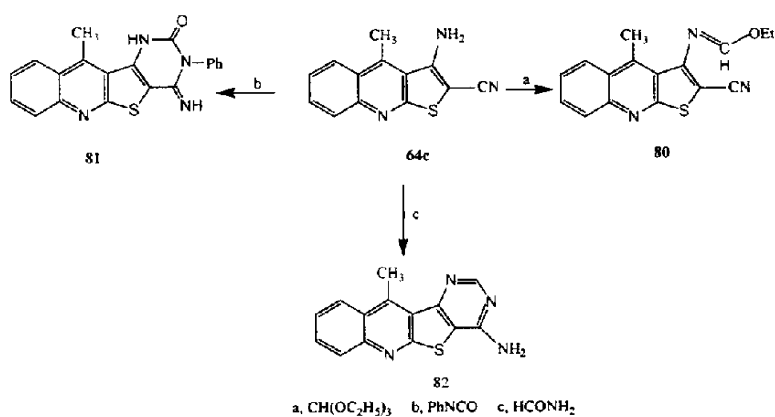
Scheme 18



Scheme 19



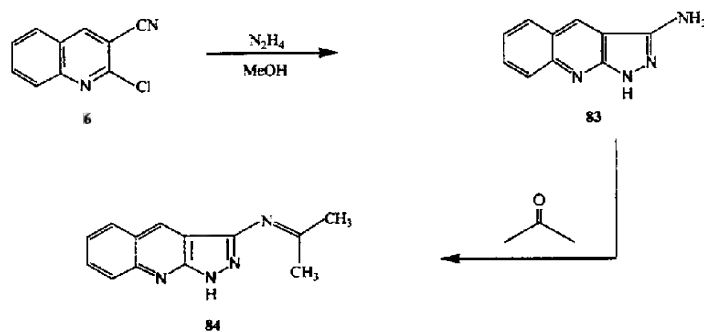
Scheme 20



Scheme 21

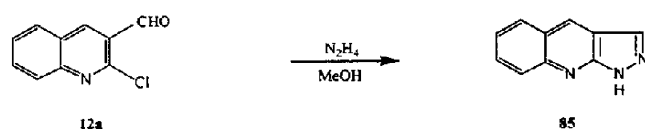
Ring closure of 2-chloro-3-cyanoquinoline (**6**) with hydrazine hydrate proceeded smoothly to yield **83** (Scheme 22).

Ring closure of 2-chloro-3-cyanoquinoline (**6**) with hydrazine hydrate proceeded smoothly to yield **83** (Scheme 22).



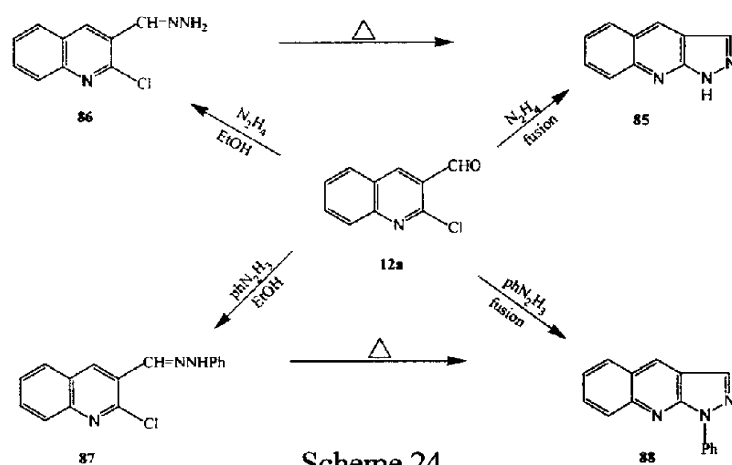
Scheme 22

It was reported⁹⁹ that on treatment of 2-chloroquinoline-3-carboxaldehyde (**12a**) with hydrazine hydrate, the pyrazolo[3,4-b]quinoline (**85**) was obtained⁹⁹ (Scheme 23).



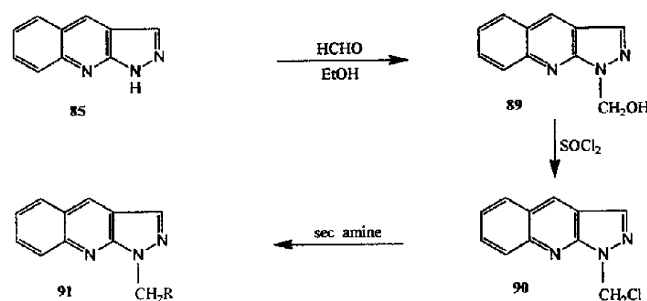
Scheme 23

The 1H-pyrazolo[3,4-b]quinoline¹⁰⁰ (**85**) was prepared by the reaction of 2-chloroquinoline-3-carboxaldehyde (**12a**) with hydrazine hydrate by fusion or by heating 2-chloro-3-formylhydrazine (**86**) above its melting point in a sealed tube. Similarly 1-phenylpyrazolo[3,4-b]quinoline (**88**) was obtained by using phenylhydrazine under the same conditions (Scheme 24).



Scheme 24

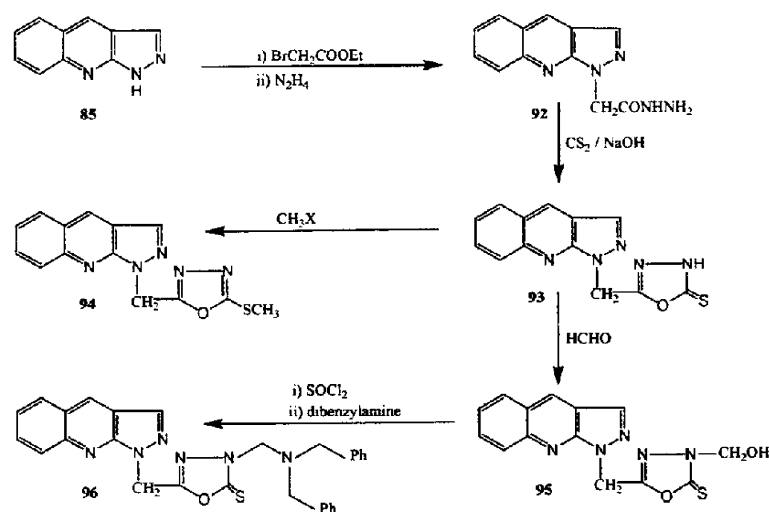
Also, 1H-pyrazolo[3,4-b]quinoline (**85**) reacted with formaline yielded 1-hydroxymethylpyrazolo[3,4-b]quinoline (**89**). The Mannich bases **91** were not performed via classical Mannich reaction but were prepared via an indirect pathway involving the formation of compound **89** at first, followed by treatment with thionyl chloride to give the unstable compound 1-chloromethylpyrazolo[3,4-b]quinoline (**90**). This latter compound **90** was reacted directly with the proper secondary amine to afford the required Mannich bases **91** (Scheme 25).



91: R=piperidino, morpholino, N-methylpiperazino, dibenzylamino

Scheme 25

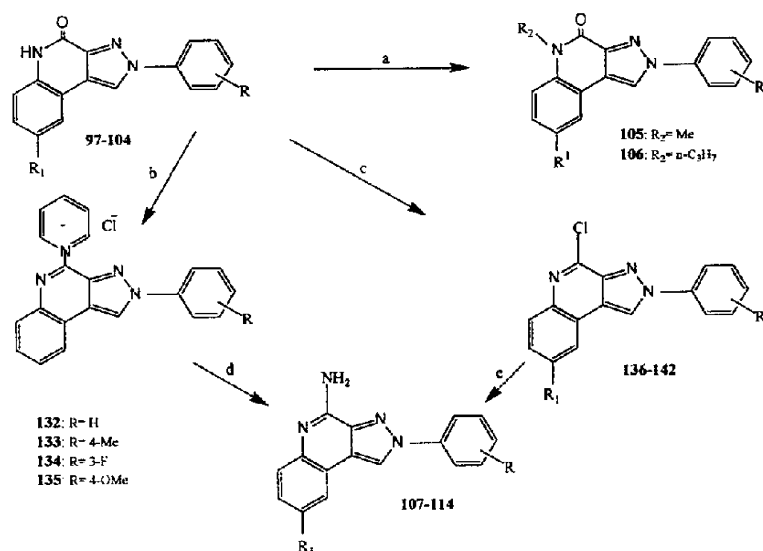
Treatment of compound **85** with ethyl bromoacetate, then with hydrazine hydrate gave the pyrazolo[3,4-b]quinoline-1-aceto hydrazide (**92**). The latter reacted with carbon disulphide and sodium hydroxide in ethanol gave 1-(5-thioxo-4H-1,3,4-oxadiazolo-2-yl)methylpyrazolo[3,4-b]quinoline (**93**). Alkylation of compound **93** with alkyl or aralkyl halide gave the corresponding alkylthio or aralkylthio derivative **94**, while its reaction with formaline afforded the corresponding N-hydroxymethyl derivative **95**, which was reacted with thionyl chloride followed by secondary amine yielded the Mannich bases 1-(4-substituted aminomethyl-5-thioxo-4H-1,3,4-oxadiazol-2-yl)-methylpyrazolo[3,4-b]quinoline (**96**) (Scheme 26).



Scheme 26

Cupta *et al*¹⁰¹ studied the synthesis and structure activity relationships of a new set of 2-arylpyrazolo[3,4-c]quinoline derivatives. The synthetic pathway which yielded compounds **97-133** are illustrated in (Schemes 27-29). The synthesis of **97**, **98**, **100-103** and **105** which were originally prepared as benzodiazepine receptor ligands has already been reported¹⁰¹. The 2-(2-methylphenyl) derivatives **99** and its 2-(4-chlorophenyl) analogue **104** were obtained by reacting the 3-ethoxallylindole¹⁰² with arylhydrazine hydrochlorides as described to prepare **97**, **98** and **100-103**. The 5-N-propyl derivative **106** ensured by the reaction of **97** with n-propyl bromide following the procedure described to prepare **102**.¹⁰¹ Reaction of **97** and **100-103** with a mixture of $\text{PCl}_5/\text{POCl}_3$ and pyridine afforded the 1-(2-aryl-2H-pyrazolo[3,4-c]quinoline-4-yl)pyridinium chlorides (**132-135**), while the reaction of **97-102** and **104** with a neat mixture of $\text{PCl}_5/\text{POCl}_3$ gave the 2-aryl-4-chloropyrazolo[3,4-c]quinolines (**136-142**). It must be noted that both the pyridinium salts **132-135** and the 4-chloro derivatives **136-142** were unstable; nevertheless they were pure enough to be spectroscopically characterized and used without further purification. Refluxing **132-135** with an excess of cyclohexylamine gave the 2-arylpyrazolo[3,4-c]quinolin-4-amines (**107 and 111-113**). Compound **107** was also obtained with more satisfactory yields from its corresponding 4-chloro derivative **136** and ammonia. Thus, the other 4-amino derivatives **108-110** and **114** were prepared following this pathway, i.e., from the corresponding 4-chloro intermediates **137-139**, **142** and ammonia (Scheme 27).

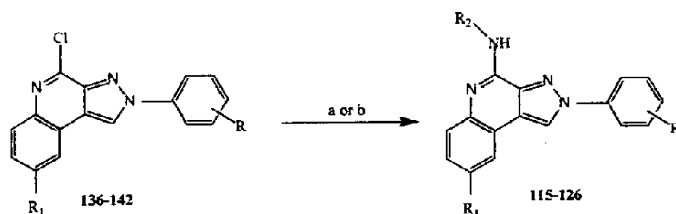
Allowing the 4-chloro intermediates **136-142** to react with suitable amines gave the 4-N-cycloalkylamines **115-124**, 4-N aralkylamines **125** and **126** (Scheme 28). Finally, Scheme 29 depicts the reaction of 2-phenylpyrazolo[3,4-c]quinolin-4-amine (**107**) with suitable acyl chlorides or phenylacetic acid, or with suitable isocyanates, to afford the 4-amido **127-129**, 4-ureido derivatives **130** and **131**, respectively.



	R	R ₁		R	R ₁
97,107,136	H	H	101, 111, 140	4-Me	H
98, 108, 137	H	Cl	102, 112, 141	3-F	H
99, 109, 138	2-Me	H	103, 113	4-OMe	H
100, 110, 139	3-Me	H	104, 114,142	4-Cl	H

(a) NaH, R₁X, DMF; (b) POCl₃, pyridine; (c) POCl₃; (d) method A: cyclohexylamine; (e) method B: NH₃(g), absolute EtOH.

Scheme 27



	R	R ₁	R ₂
115	H	H	
116	H	Cl	
117	3-Me	H	
118	4-Me	H	
119	3-F	H	
120	4-Cl	H	
121	H	H	
122	2-Me	H	
123	3-Me	H	
124	3-F	H	
125	H	H	CH ₂ Ph
126	H	H	(CH ₂) ₂ Ph

(a) Method A: excess of R₂NH₂; (b) method B: R₂NH₂, Et₃N, absolute EtOH.

Scheme 28

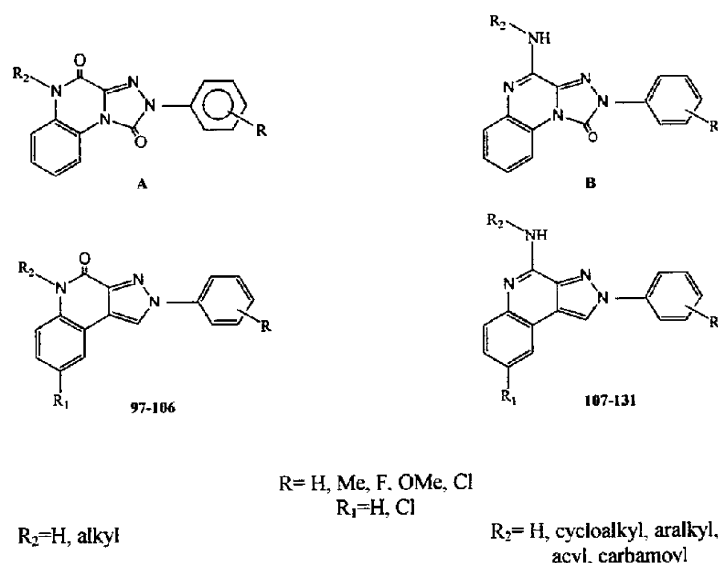


	R ₂
127	COMe
128	COPh
129	COCH ₂ Ph
130	CONHPh
131	CONHCH ₂ Ph

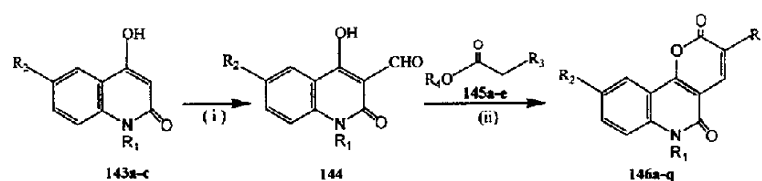
(a) RCOCl, pyridine, CH₂Cl₂; (b) PhCH₂COOH, 1-hydroxybenzotriazole, Et₃N(dimethylamino)pyridine, 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride, DMF; (c) RNCO, THF.

Scheme 29

Chart 1. Previously and Hereby Reported Adenosine Receptor Antagonists



2,5-Dioxo-5,6-dihydropyrano[3,2-c]quinolines¹⁰² were prepared by Junek *et al.*¹⁰² They present a convenient synthesis for substituted 2,5-dioxo-5,6-dihydropyrano[3,2-c]quinolines (**146_{a-p}**) in good yield by using the Knoevenagel reaction and cyclization in the presence of mild base. To synthesize pyrano[3,2-c]quinolines (**146_{a-p}**), 4-hydroxy-3-formylquinolin-2-ones (**144_{a-c}**) were considered as versatile bifunctional starting materials. **144_{a-c}** were prepared by adopting Riemer-Tiemann reaction. 4-Hydroxy-3-formyl-1-methylquinolin-2-one (**144_a**) was treated with phenyl acetic acid in acetic anhydride in the presence of triethylamine at steam bath for 2h. After usual work up and purification, the corresponding 3-phenyl-6-methyl-2,5-dioxo-5,6-dihydropyrano[3,2-c]quinoline (**146_a**) was obtained. The other 4-hydroxy-3-formylquinolin-2(1H)-ones (**143_{a-c}**) were reacted similarly with a variety of active methylene compounds (**145_{a-f}**) to yield the corresponding 2,5-dioxo-5,6-dihydropyrano[3,2-c]quinolines (**146_{b-p}**). 6-Methyl-2,5-dioxo-5,6-dihydropyrano[3,2-c]quinoline (**146_q**) was obtained by Perkin reaction of **143_a** with acetic anhydride in the presence of anhydrous sodium acetate. The substituted pyrano[3,2-c]quinolines exhibited remarkable fluorescence.¹⁰³⁻¹⁰⁴ The mechanism for the formation of **146_{a-p}** could involve, the carbanion derived from the active methylene compounds **145_{a-f}** may be considered to attack the carbonyl group without further interaction of base and the subsequent intramolecular ring closure lead to pyrano[3,2-c]quinolines.



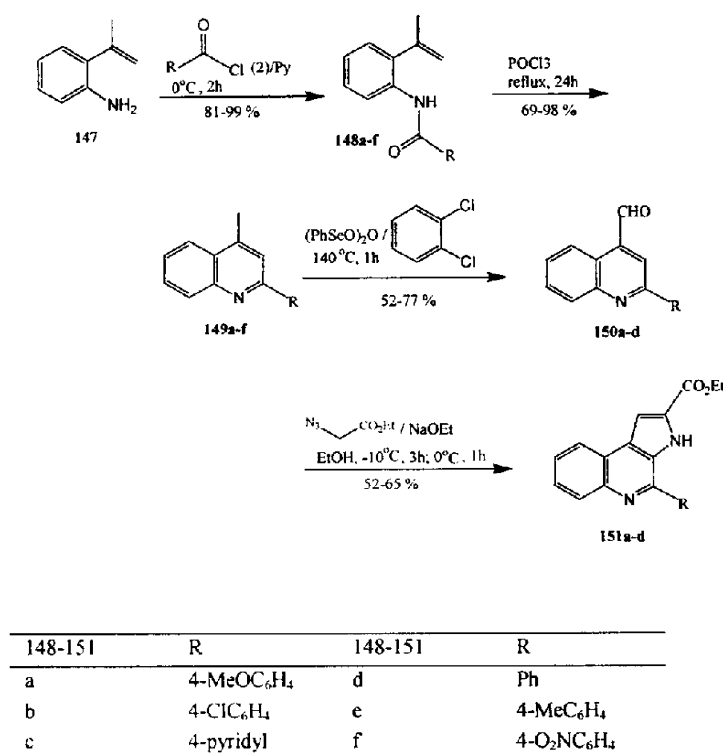
(i) 15% NaOH / CHCl₃; (ii) Ac₂O / Base

Entry	R ¹	R ²	R ³	R ⁴	Base
144 _a	CH ₃	H	-	-	-
144 _b	C ₆ H ₅	H	-	-	-
144 _c	CH ₃	Br	-	-	-
145 _a	-	-	C ₆ H ₅	H	-
145 _b	-	-	p-OCH ₃ C ₆ H ₄	H	-
145 _c	-	-	CO ₂ C ₂ H ₅	C ₂ H ₅	-
145 _d	-	-	CONHC ₆ H ₅	H	-
145 _e	-	-	NHCOCH ₃	H	-
145 _f	-	-	COCH ₃	C ₂ H ₅	-
145 _g	-	-	H	CH ₃ CO	-
146 _a	CH ₃	H	C ₆ H ₅	-	TEA
146 _b	C ₆ H ₅	H	C ₆ H ₅	-	TEA
146 _c	CH ₃	Br	C ₆ H ₅	-	TEA
146 _d	CH ₃	H	p-OCH ₃ C ₆ H ₄	-	TEA
146 _e	C ₆ H ₅	H	p-OCH ₃ C ₆ H ₄	-	TEA
146 _f	CH ₃	Br	p-OCH ₃ C ₆ H ₄	-	TEA
146 _g	CH ₃	H	CO ₂ C ₂ H ₅	-	TEA
146 _h	C ₆ H ₅	H	CO ₂ C ₂ H ₅	-	TEA
146 _i	CH ₃	Br	CO ₂ C ₂ H ₅	-	TEA
146 _j	CH ₃	H	CONHC ₆ H ₅	-	TEA
146 _k	C ₆ H ₅	H	CONHC ₆ H ₅	-	TEA
146 _l	CH ₃	Br	CONHC ₆ H ₅	-	TEA
146 _m	CH ₃	H	NHCOCH ₃	-	piperidine
146 _n	C ₆ H ₅	H	NHCOCH ₃	-	piperidine
146 _o	CH ₃	Br	NHCOCH ₃	-	piperidine
146 _p	CH ₃	H	COCH ₃	-	piperidine
146 _q	CH ₃	H	H	-	NaOAc

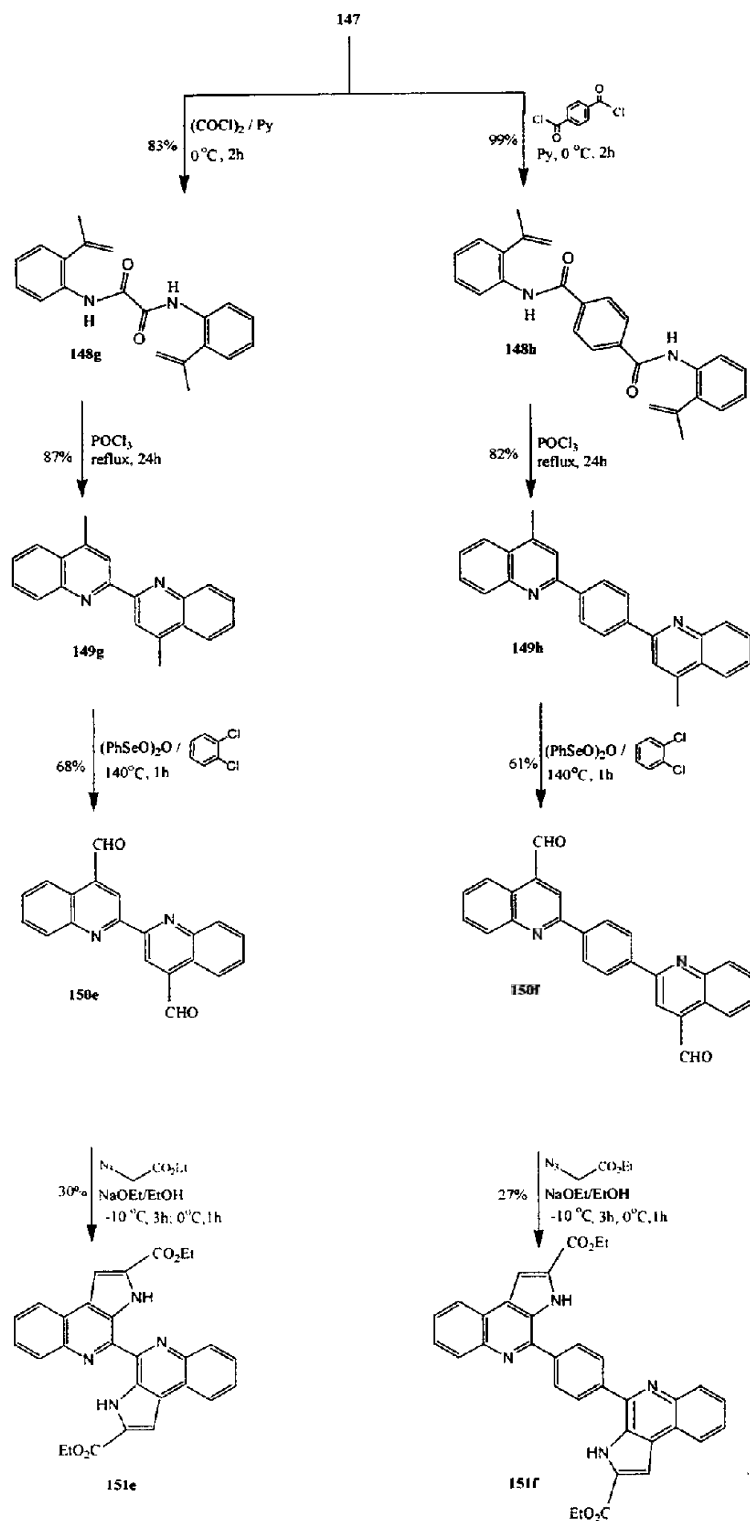
Scheme 30

A number of ethyl 3H-pyrrolo[2,3-c]quinoline-2-carboxylates¹⁰⁵ have been prepared directly by condensation of ethyl azidoacetate with 4-formylquinolines, the procedure is based on the known thermal decomposition of α -azido acrylate bearing a β -aryl or heteroaryl substituent to give fused pyrroles. However, this method has been applied for the annulation of a pyrrole ring into a performed benzene,¹⁰⁶ thiophen,¹⁰⁷ furan¹⁰⁸ and indol ring¹⁰⁹ and no example dealing with annulation into quinoline ring. The key intermediate 4-formylquinolines (**150**) have been prepared from α -(1-

methylethenyl)aniline¹¹⁰ by sequential treatment with acid chlorides and phosphorous oxychloride¹¹¹ followed by oxidation with benzeneseleninic anhydride¹¹² of the resulting 4-methylquinolines (149). Thus aniline derivative 147 reacts with acid chlorides in pyridine at 0°C leading to the corresponding amides 148 in excellent yields. When compounds 148 are treated with neat freshly distilled phosphorus oxychloride at reflux temperature, the corresponding 2-substituted 4-methylquinolines (149) are obtained. The oxidation of 149 into 4-formylquinolines is achieved by treatment with benzeneselenenic anhydride in 1,2-dichlorobenzene. Treatment of compound 150 with ethyl azidoacetate in ethanol in presence of sodium ethoxide at -10 °C under nitrogen leads directly to 3H-pyrrolo[2,3-c]quinoline derivatives (151) (Scheme 31, 32).

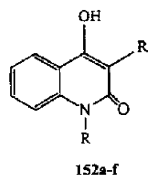


Scheme 31

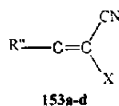




Scheme 32

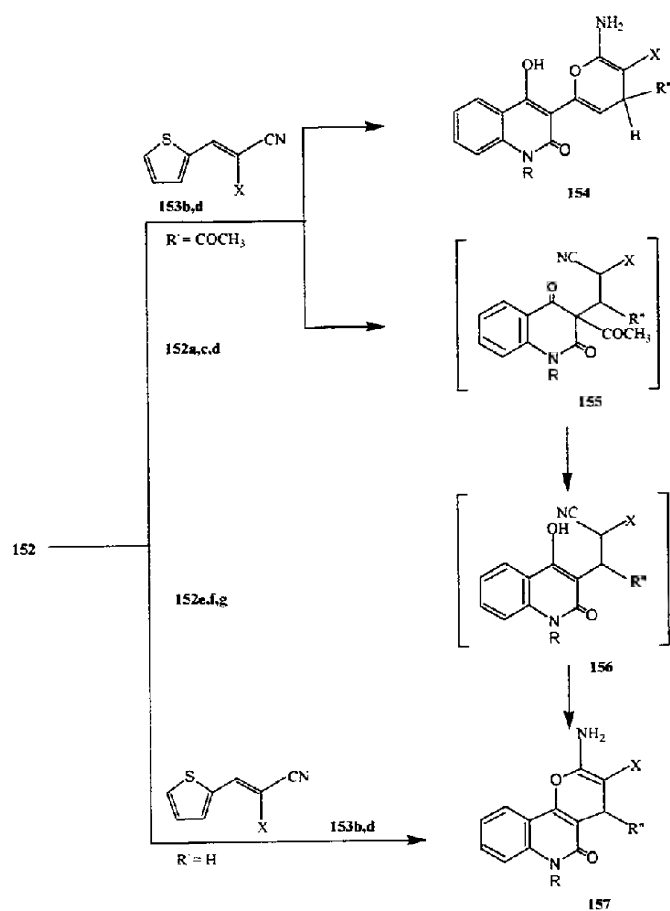
Several new 4H-pyran[3,2-c]quinolines¹¹³⁻¹¹⁹ were prepared from the reaction of 4-hydroxy-2-(1H)quinolinones (**152**) and ylidene nitriles (**153**). Compounds **160** were prepared from the reaction of 1-ethylidenemalononitrile (**153_e**) with **152_{c,d}** or **152_{f,g}**. Reaction of pyrano[3,2-c]quinoline (**161**) with **153_a** or **153_c** afforded benzo[b]pyrano[3,2-c]quinolines (**162** and **163**) respectively. Treatment of **152_{b,c}** with malononitrile and elemental sulfur yields **167**.



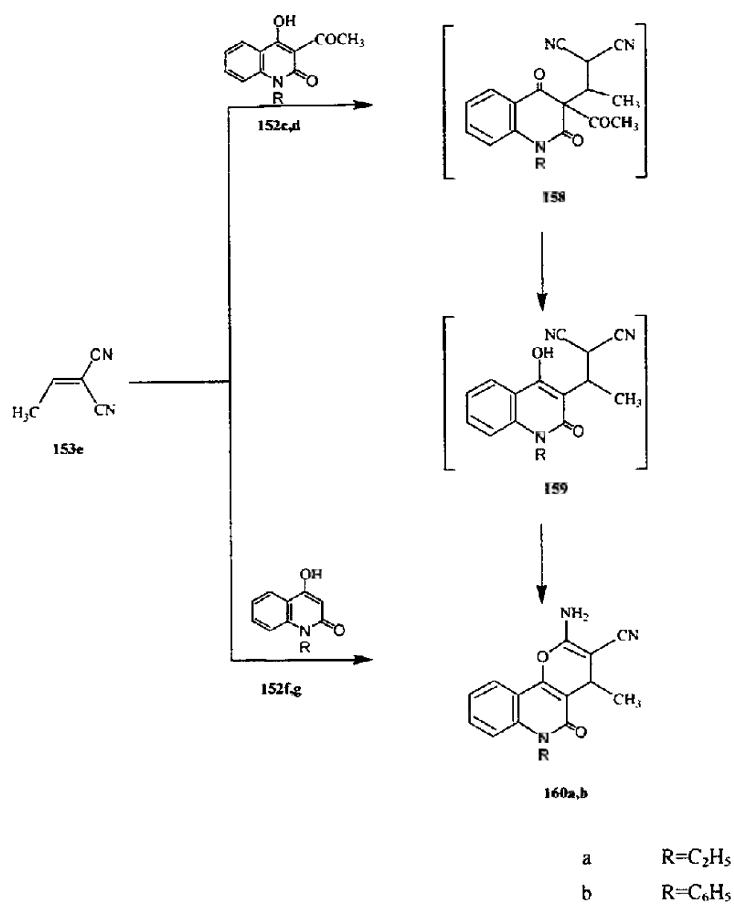
152 a	R= H	R' = COCH ₃	152 b	R= CH ₃	R' = COCH ₃
152 c	R= C ₂ H ₅	R' = COCH ₃	152 d	R= C ₆ H ₅	R' = COCH ₃
152 e	R= H	R' = H	152 f	R= C ₂ H ₅	R' = H
152 g	R= C ₆ H ₅	R' = H			



153 a	R'' = C ₆ H ₅ ; X= CN	153 b	R'' =  ; X= CN
153 c	R'' = C ₆ H ₅ ; X= CO ₂ C ₂ H ₅	153 d	R'' =  ; X= CO ₂ C ₂ H ₅
152 e	R'' = CH ₃ ; X= CN		

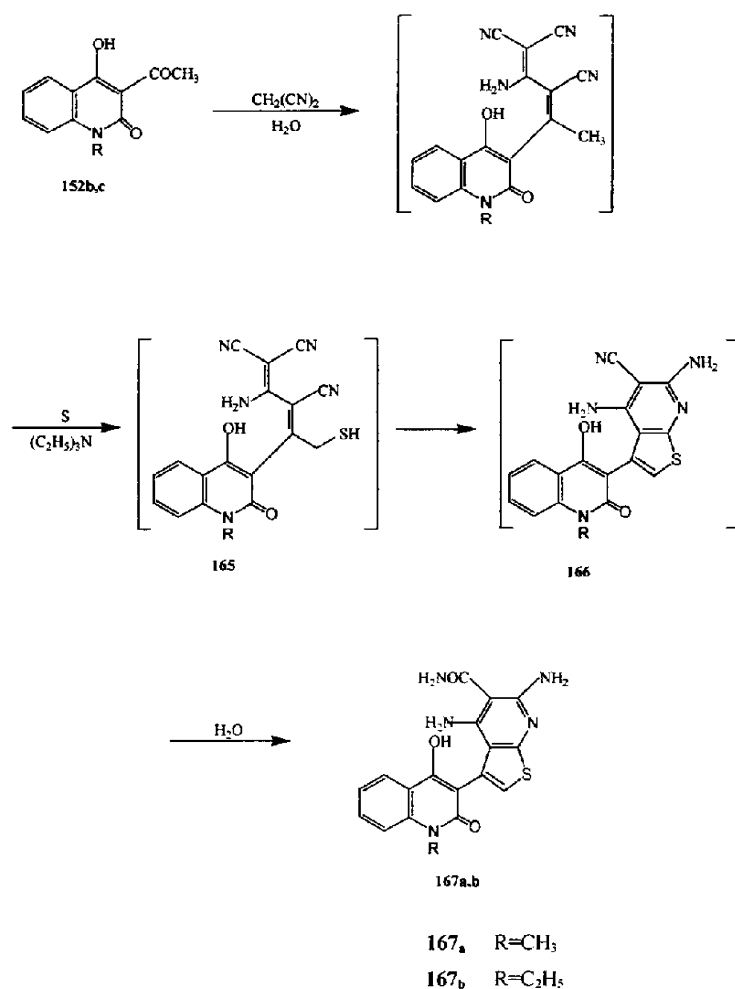


157	R	R''	X
a	H		CN
b	C ₂ H ₅	"	"
c	C ₆ H ₅	"	"
d	H	"	CO ₂ C ₂ H ₅
e	C ₂ H ₅	"	"
f	C ₆ H ₅	"	"



Scheme 33

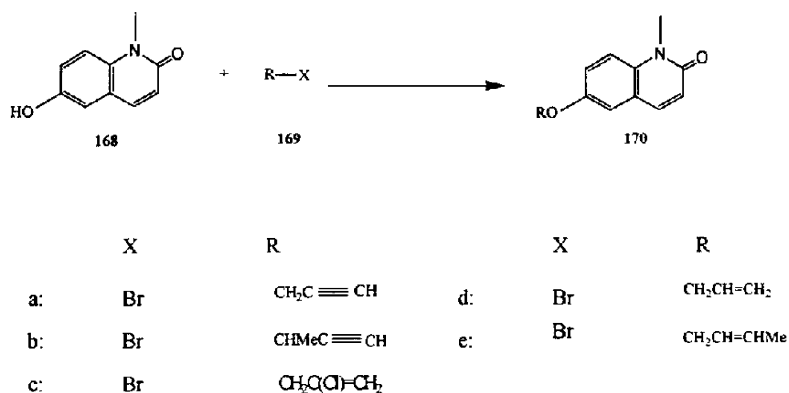




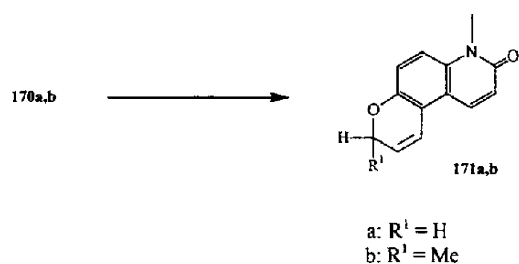
Scheme 35

Pyrano[3,2-f]quinolin-2(7H)-one and furo[3,2-h]quinolin-2-one was accomplished via a thermal[3,3]-sigmatropic rearrangement by Majumdar *et al.*¹²⁰

The starting materials **170_{a-e}** were synthesized by treating 6-hydroxy-1-methylquinoline-2(H)-one (**168**) with different propynylic and allylic halides (**169**) in refluxing acetone in the presence of anhydrous potassium carbonate. A thermal [3,3]-sigmatropic rearrangement was utilized for the synthesis of the pyrano-and furano-quinolines. The pyrano[3,2-f]quinolin-2(7H)-ones (**171a,b**) were obtained by heating the propynyl ethers **170a,b** in refluxing N,N-diethylaniline.

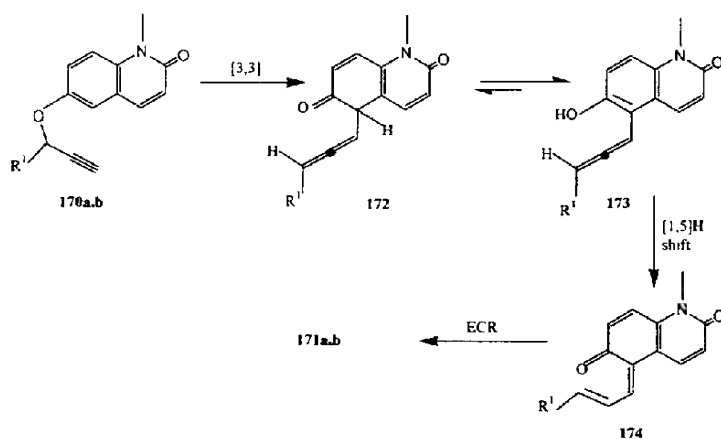


Scheme 36



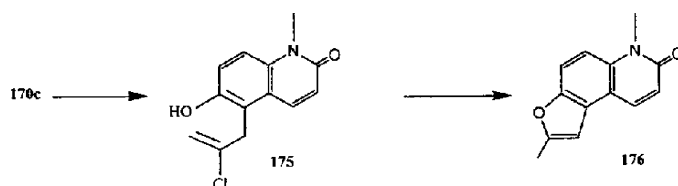
Scheme 37

The formation of pyrano[3,2-f]quinoline-2(7H)-ones (**171_{a,b}**) may be rationalized by the initial [3,3]-sigmatropic rearrangement of the propynyl ethers **170_{a,b}** to the allenyl derivatives **172** followed by enolization, [1,5]-hydrogen shift, and electrocyclic ring closure¹²¹ to give the products **171_{a,b}**.

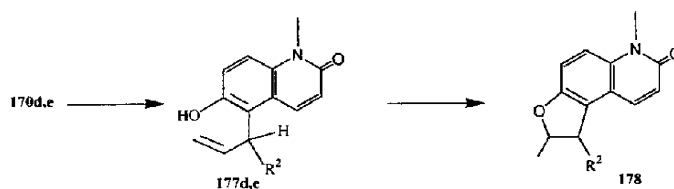


Scheme 38

The furo[3,2-f]quinolin-2-one derivatives **176** and **178** were synthesized via two different routes. In one route, the chloropropenyl ether **170c** was heated in refluxing N,N-diethylaniline for 12h to give the corresponding chlorallyl enol **175** which was easily cyclized to the corresponding 1,6-dimethylfuro[3,2-f]quinolin-2-one **176** in 80 % yield when treated with 20 % alcoholic KOH for 3h. (Scheme 39).



Scheme 39

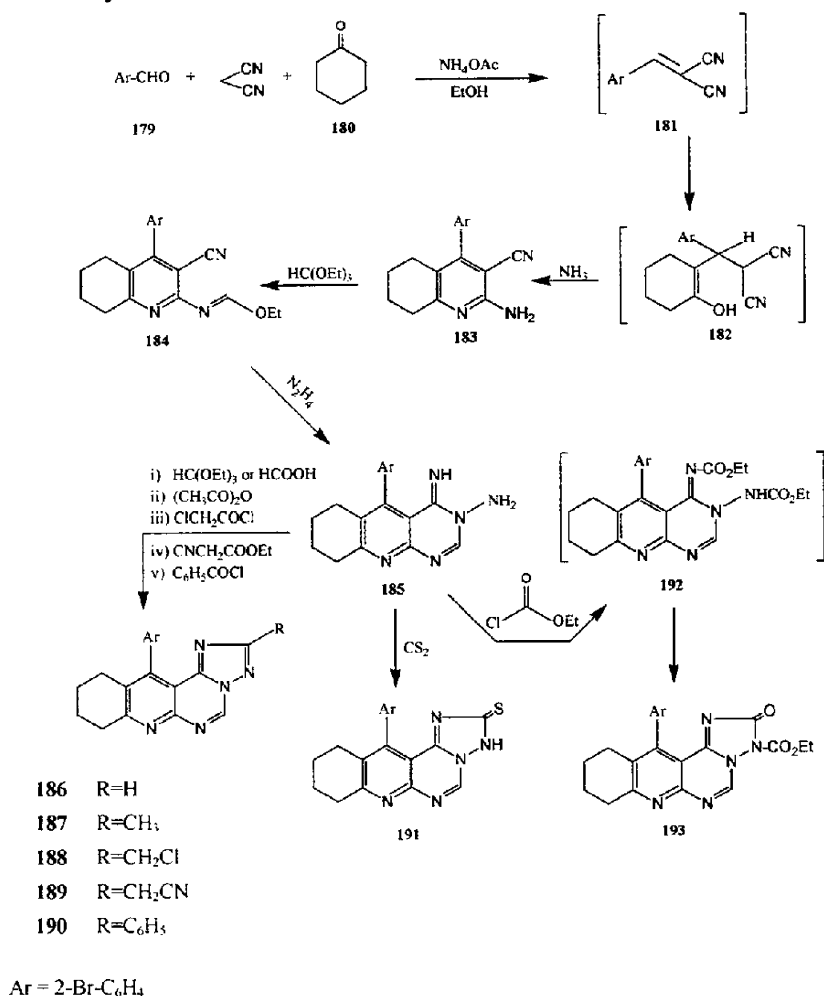


177_d $R^2=H$

177_e $R^2=Me$

Scheme 40

Ghorab *et al*¹²² reported that 2-alkyl(or aryl)-12-(2-bromophenyl)-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinolines of potential biochemical activity have been synthesized.



Scheme 41

The starting material, 2-amino-4-(2-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (**183**) was synthesized by the reaction of 2-bromobenzaldehyde (**179**), malononitrile and cyclohexanone (**180**) in equimolar proportions in the presence of ammonium acetate. The formation of 2-amino-4-(2-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (**183**) was rationalized in terms of the initial formation of benzyldenemalononitrile (**181**) followed by the addition of cyclohexanone to the ylidenic bond forming acyclic intermediate **182**. Amination of **182** in the presence of ammonium acetate followed by cyclization of the

enamine and partial dehydrogenation under the reaction conditions afforded the final product **183** (Scheme 41). This was confirmed through equimolar condensation of **181** and **180** under the previous conditions, which also afforded **183**.

Treatment of **183** with triethyl orthoformate gave 2-ethoxymethylenamino-4-(2-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (**184**), which reacted with hydrazine hydrate at room temperature to yield the 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-3-amine (**185**).

A combination of the pyrimidinoquinoline system with a triazole moiety was afforded through the condensation of 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-3-amine **185** with various acid chloride and ester derivatives.

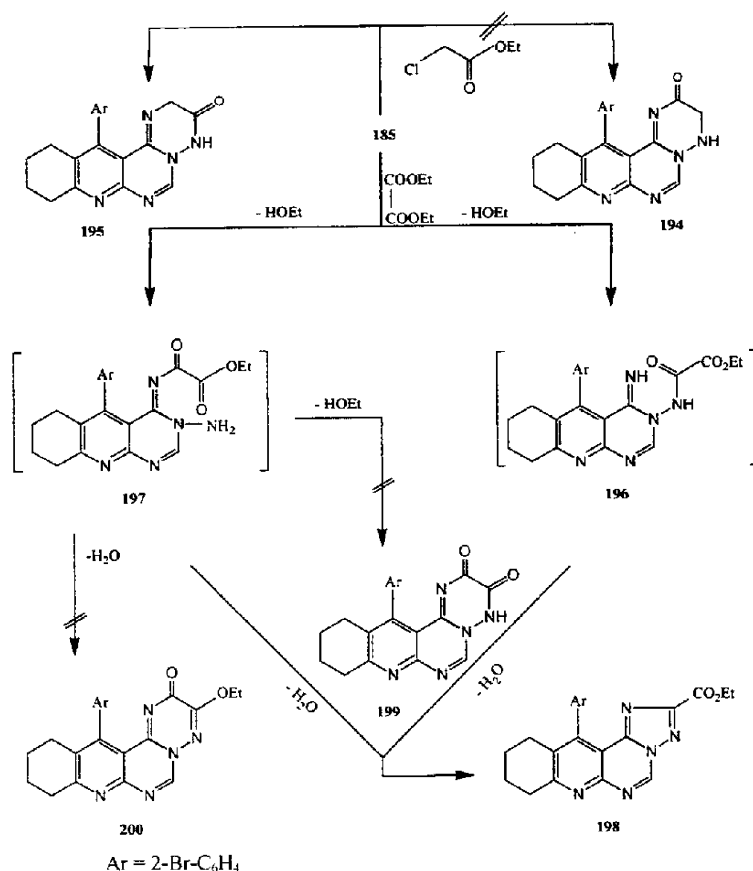
Treatment of compound **185** with chloroacetyl chloride and / or ethyl cyanoacetate yielded the corresponding 12-(2-bromophenyl)-2-chloromethyl-8,9,10,11-tetrahydro-[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline (**188**) and 12-(2-bromophenyl)-2-cyanomethyl-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline (**189**) respectively, while with carbon disulphide, the 12-(2-bromophenyl)-2-thioxo-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline (**191**) was obtained.

Condensation of **185** with ethyl chloroformate afforded ethyl 12-(2-bromophenyl)-2-oxo-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline-3-carboxylate (**193**).

When **185** was refluxed with triethyl orthoformate or formic acid, it afforded the corresponding 12-(2-bromophenyl)-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]-pyrimido[4,5-b]quinoline (**186**), whereas with acetic anhydride or benzoyl chloride, the respective 12-(2-bromophenyl)-2-methyl-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline (**187**) and 12-(2-bromophenyl)-2-phenyl-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline (**190**), were obtained.

Reaction of 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydro-pyrimido[4,5-b]-quinoline-3-amine (**185**) with ethyl chloroacetate in refluxing sodium methoxide solution yielded the triazinopyrimidoquinoline derivative **195** rather than its isomeric structure **194** (Scheme 42). Structure **195** was suggested rather than structure **194**, based on assumption that the reaction basic condition allowed it to proceed through formation of sodium salt on the less basic imino nitrogen atom, and elimination of

sodium chloride followed by cyclization **192**. In addition, the IR spectrum of the isolated product showed a carbonyl band at 1660 cm^{-1} , which was at less frequency than that expected for structure **194**. Further evidence was the $^1\text{H-NMR}$ spectrum which showed a singlet at 4.3 ppm for the methylene protons.



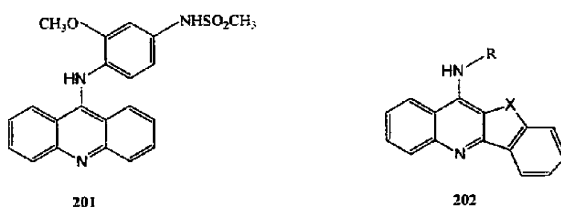
Scheme 42

Interaction of compound **185** with diethyl oxalate gave a triazolopyrimidoquinoline derivative **198**. This was confirmed by its elemental analysis, $^1\text{H-NMR}$ and mass spectra. These results are in agreement with the method previously reported **195**.

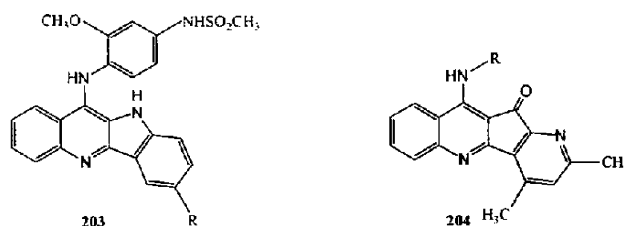
Biochemical screening of some of the synthesized compounds revealed that quinoline derivative **184** showed a significant increase in SGPT and SGOT activities. On the other hand, triazinopyrimidoquinoline derivative **195** significantly decreased serum creatinine.

Barret¹²³ reported the synthesis of new tetracyclic compounds **204** and studied the relation between the substitution of the aromatic substituent and the cytotoxic activity.

Some analogs **202** of amsacrine¹²⁴ **201** with a tetracyclic quinoline structure and an amine moiety R as a side chain, have been synthesized.¹²⁵ These authors have shown that the cytotoxic activity is dependant upon R and X. The best activity was obtained when X was a methylene group, an oxygen or a sulfur atom and R an arylamino group bearing an electron-withdrawing substituent such as NHSO_2CH_3 . These compounds are active against KB-cells (in vitro and in vivo), P388 leukemia and various solid tumors.¹²⁶



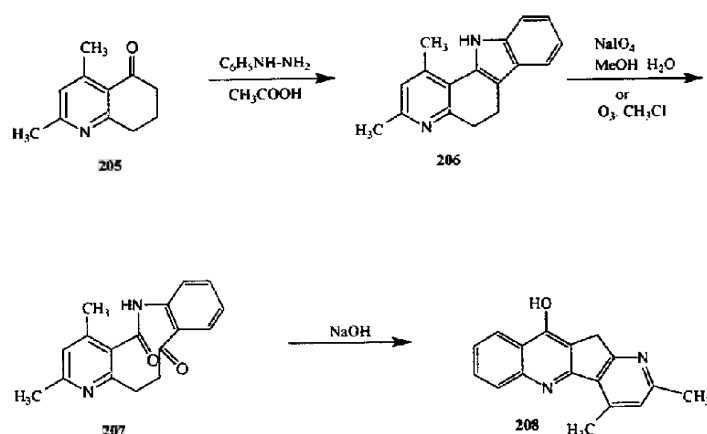
Chang has synthesized indolo[3,2-b]quinolines¹²⁷ (**203**). These compounds are cytotoxic against leukemia P388 in mice, in particular when R is a galactopyranosyl moiety.



In this work he has synthesized new tetracyclic compounds **204** and studied the relation between the substitution of the aromatic substituent and the cytotoxic activity.

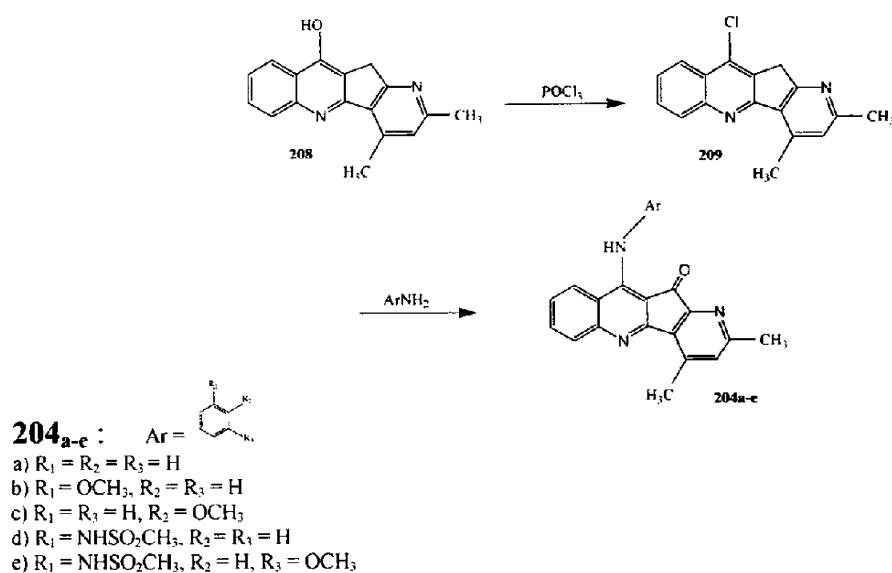
The 5-oxo-2,4-dimethyltetrahydroquinoline¹²⁸ (**205**) was reacted with phenylhydrazine (Fisher reaction) to give the tetracyclic compound **206**, which led to the ketolactam **207** by either ozonolysis or periodate oxidation. Compound **208** was obtained by cyclization in alkaline medium.¹²⁹ Compound **206** is unstable and must be

used immediately after preparation. It is quickly oxidized to a 5,6-dehydrogenation product (Scheme 43).



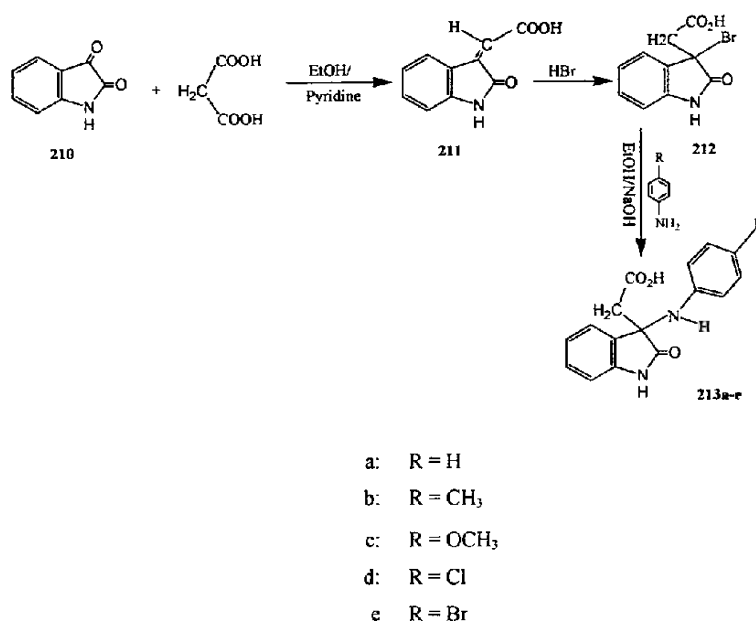
Scheme 43

The chloro derivative **209** was obtained by treatment of **208** with phosphoryl chloride (Scheme 44). At this point, different amines were condensed with **209**. Stirring **209** at room temperature with the appropriate amine in methanol afforded **204** after 15 days in low yield. Heating of these solutions at a reflux temperature led only to degradation products. Other procedures such as stirring the solution of **209** and amines in N-methyl-2-pyrrolidinone,^{130a} heating at 100 °C in phenol in the absence^{130b} or in the presence of potassium iodide^{130c} or at reflux in ethanol,^{130d} did not give the expected products. Finally, improvement was obtained by the use of Andersen's process (reflux in 2-methoxyethanol instead of 2-ethoxyethanol).¹³¹



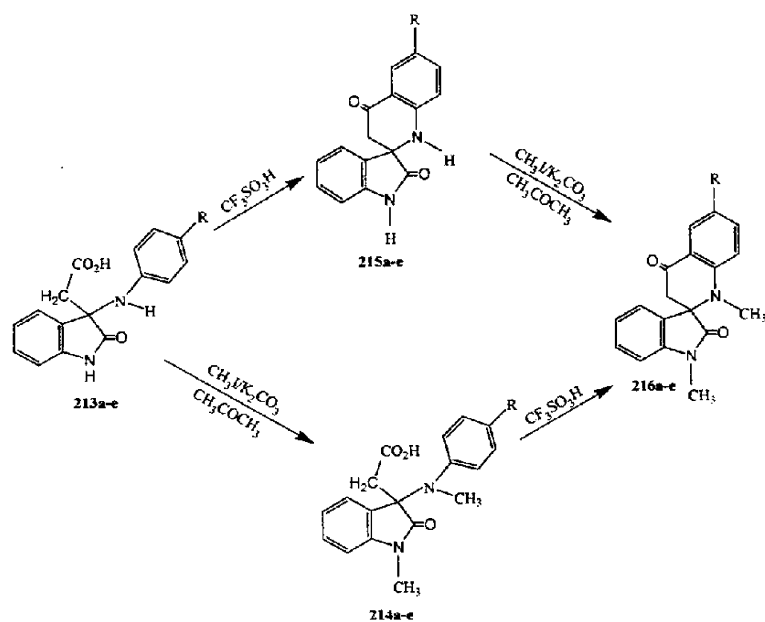
Scheme 44

New spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinoline)]-2,4'-dione¹³²(**216_{a-e}**) derivatives were prepared according to the following:



Scheme 45

Reaction of compounds **213a-e** with triflic acid yielded the target cyclodehydration products; spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinoline)]-2,4'-dione derivatives **215a-e** (Scheme 46). Alkylation of compounds **213a-e** with methyl iodide and anhydrous potassium carbonate in dry acetone afforded 3-arylmethylamino-3-(1-methyl-2-oxoindole) acetic acid derivatives **214a-e** in good yield. The reaction of compounds **214a-e** with triflic acid yielded spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinoline)]-1,1'-dimethyl-2,4'-dione derivatives **216a-e** in good yields (Scheme 46). For the rigid identification of compounds **216a-e**, unequivocal syntheses for **216a-e** were established by the alkylation of compounds **215a-e** with methyl iodide.



213a-e-216a-e

- a: R = H
- b: R = CH_3
- c: R = OCH_3
- d: R = Cl
- e: R = Br

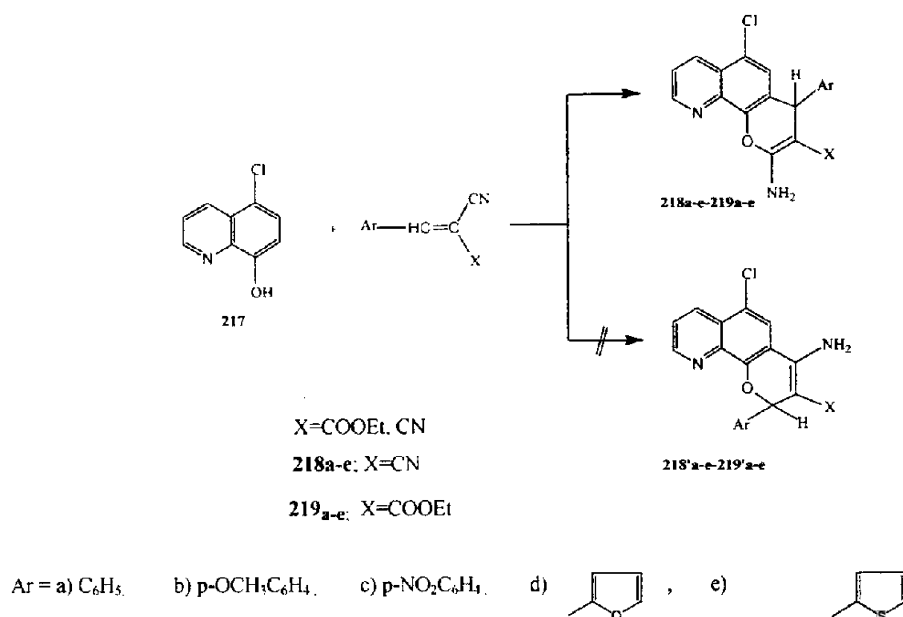
Scheme 46

Results and Discussion

RESULTS AND DISCUSSION

The pyran ring system is an interesting class of heterocycles. It has been reported that pyran derivatives exhibit antimicrobial activities,¹³³ growth stimulating effects,⁴⁰ antifungal and plant growth regulation effects,³⁷ antitumor activity,³⁸ central nervous system activity⁴⁵ and hypotensive⁴⁴ effect. On the other hand, fused pyrimidines were found to possess a wide biological activities such as antimicrobial⁴⁹ antiparkinsonion⁵¹ leishmanicidal and herbicidal.⁵⁵ Moreover, quinoline derivatives have found useful applications as antimicrobial,¹³³ antimalarial,¹³⁵ cardiovascular and biochemically active compounds.¹³⁶ In addition to the previously mentioned properties, many imidazoles and triazines are used as therapeutic tools.^{62,63,81} Based on these findings, it was of interest to introduce these biologically active moieties in one molecule, giving rise to a new series of potentially biochemically active compounds.

It has been found that 5-chloro-8-quinolinol (**217**) reacts with the ylidene nitriles in ethanol and in the presence of catalytic amount of piperidine for which two products **218_{a-c}**-**219_{a-c}** and **218'_{a-c}**-**219'_{a-c}** seemed possible.^{113, 137-140} Structures **218_{a-c}**-**219_{a-c}** were established for the reaction products based on ¹H-NMR spectra which revealed the presence of a 4H-pyran proton at $\delta=4.80-5.10$ ppm, thus structures **218'_{a-c}**-**219'_{a-c}** were readily ruled out^{137,138} (Scheme 47).

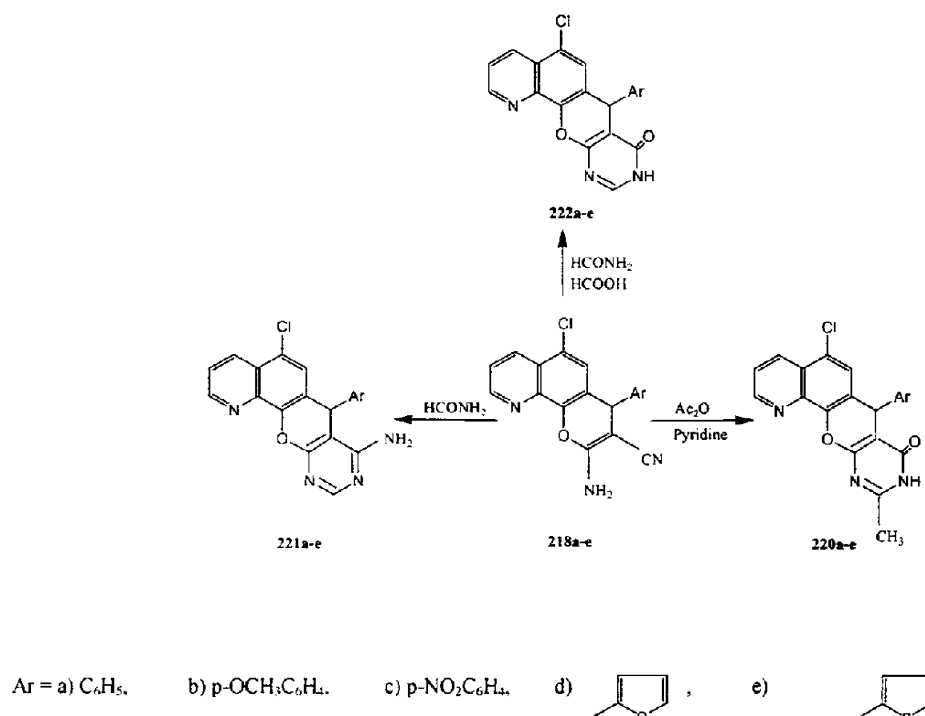


Scheme 47

The structures of compounds **218_{a-e}** - **219_{a-e}** namely 2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines and Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]-quinoline-3-carboxylates, respectively were established from their elemental analysis and spectroscopic data. The IR (KBr, ν cm^{-1}) spectrum showed the absorptions bands at 3324-3180 (NH_2), 2192 (CN) for compound **218_a** and at 3473-3273 (NH_2), 1731 (CO) for compound **219_a**. The $^1\text{H-NMR}$ (CDCl_3 , δ ppm) spectrum showed the following signals: 4.90 (1H, s, pyran ring), 8.80 (2H, s, NH_2) and 6.90-8.10 (9H, m, arom.) for compound **218_a** and at 5.10 (1H, s, pyran ring), 1.30 (3H, t, CH_3), 4.20 (2H, q, CH_2), 8.90 (2H, s, NH_2) and 7.80-8.50 (9H, m, arom.) for compound **219_a** (cf. fig. 3).

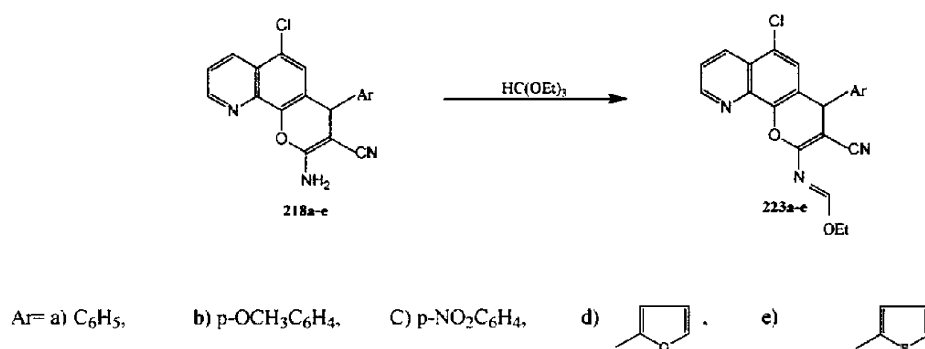
Compounds **218_{a-e}** proved to be a useful key intermediate in the synthesis of fused heterocyclic systems. Thus the pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**220_{a-e}** - **222_{a-e}**) were produced when compounds **218_{a-e}** were reacted with acetic anhydride / pyridine mixture, formamide and formamide/formic acid mixture respectively.

The IR (KBr, ν cm^{-1}) spectrum showed the absorption bands at 3391 (NH), 1690 (CO) for **220_a** ; 3440-3340 (NH_2) for **221_a** and 3100 (NH), 1690 (CO) for **222_a** respectively (Scheme 48).



Scheme 48

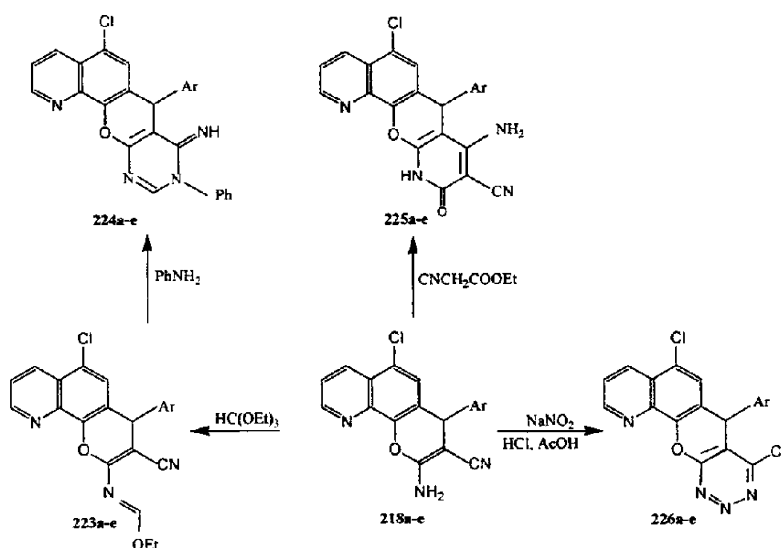
4-Aryl-3-cyano-6-chloro-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]quinolines (**223_{a-e}**) were obtained by refluxing compounds **218_{a-e}** with triethylorthoformate. The IR spectrum of compound **223_a** showed band at 2208 cm^{-1} due to the cyano group with the disappearance of the characteristic band due to the amino group. The $^1\text{H-NMR}$ spectrum (CDCl_3 , δ ppm) shows a new triplet at 1.65 ppm and quartet at 4.20 ppm, which are assigned to CH_3 and CH_2 of the ethoxy group beside the expected signals of the rest of the molecule (Scheme 49).



Scheme 49

Compounds **223_{a-e}** underwent aminolysis and cyclization by treatment with aniline to give in "one step reaction" 7-aryl-5-chloro-8-imino-9-phenylpyrimido[4',5':6,5]-pyrano[3,2-h]quinolines (**224_{a-e}**). The $^1\text{H-NMR}$ data (absence of signals due to ethoxy group) support the formation of these compounds.


The interaction of **218_{a-e}** with ethyl cyanoacetate led to the formation of 8-amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano[3,2-h]quinolines (**225_{a-e}**). The structure was established by elemental analyses and spectral data such as the appearance of new characteristic absorption bands in the IR spectrum at $3334\text{--}3201\text{ cm}^{-1}$ and 2203 cm^{-1} attributable to the amino and cyano groups respectively.



Ar = a) C_6H_5 ,

b) $\text{p-OCH}_3\text{C}_6\text{H}_4$,

c) $\text{p-NO}_2\text{C}_6\text{H}_4$,

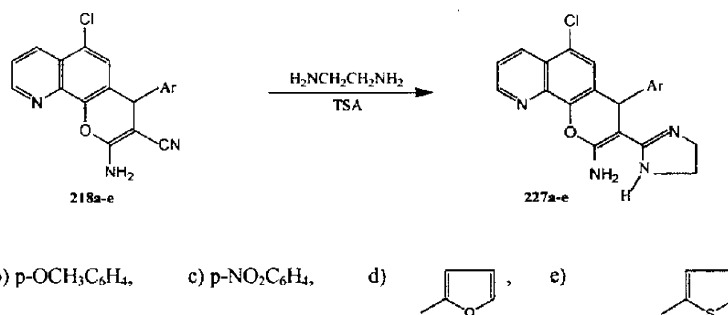
d) ,

e) 

Scheme 50

The $^1\text{H-NMR}$ (CF_3COOD , δ ppm) spectrum of **225a-e** showed signals at 4.95 (1H, s, pyran) and 7.00-8.10 (9H, m, arom.). Furthermore, compounds **218a-e** gave the corresponding triazine derivatives **226a-e** by means of diazotization with sodium nitrite in a mixture of hydrochloric and acetic acid (Scheme 50); all compounds were identified by conventional methods such as elemental and spectral analyses. The IR spectrum showed the disappearance of absorption bands due to the amino and cyano groups.


2-Amino-4-aryl-3(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]quinolines (**227a-e**) were prepared by the reaction of the pyranoquinolines **218a-e** with ethylenediamine (Scheme 51).



Ar = a) C_6H_5 ,

b) $\text{p-OCH}_3\text{C}_6\text{H}_4$,

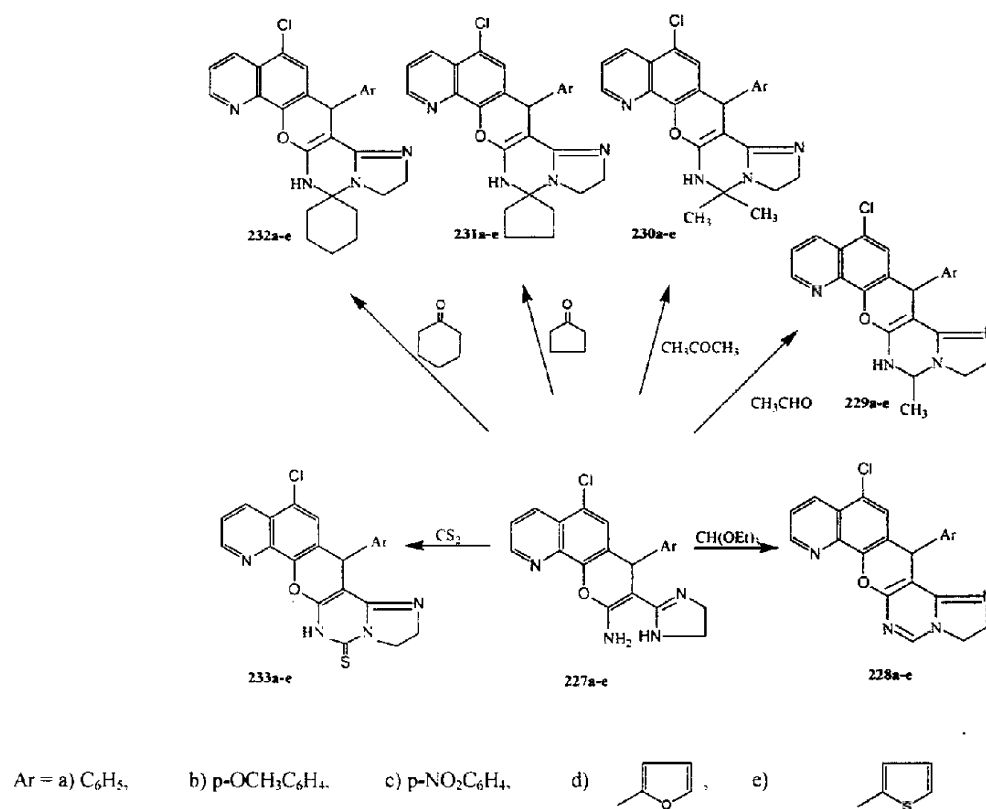
c) $\text{p-NO}_2\text{C}_6\text{H}_4$,

d) ,

e) 

Scheme 51

The structure of compounds **227_{a-e}** were confirmed by their elemental analyses and spectral data (cf. experimental section). The IR spectrum showed a new absorption band at 3437 cm^{-1} due to NH and the $^1\text{H-NMR}$ spectrum showed a new signal as a singlet at 8.95 ppm due to NH proton and two triplets at 3.30, 3.90 ppm which are assigned to imidazolyl-H atoms, beside the absorption bands and signals of the rest of the molecule. Compounds **227_{a-e}** serve as intermediate for the synthesis of imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines. Thus the cyclization of compounds **227_{a-e}** with triethyl orthoformate, aldehydes and ketones gave the corresponding 2,3-dihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**228_{a-e}**) and 2,3,5,6-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**229_{a-e}**-**230_{a-e}**) while the reaction with cyclic ketones and carbon disulfide gave spiroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**231_{a-e}**-**232_{a-e}**) and 5-thioxo-2,3,6-trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**233_{a-e}**) respectively (Scheme 52).



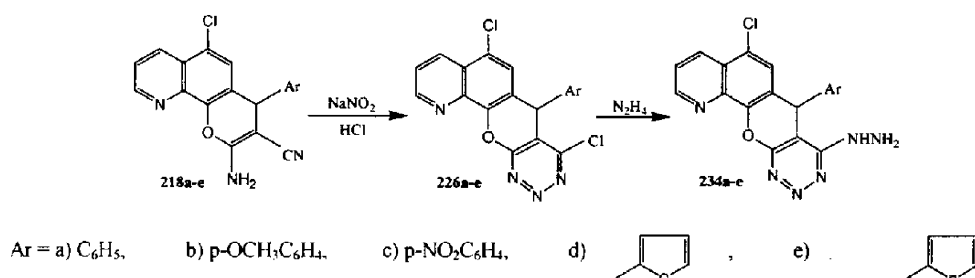
Scheme 52

The structures of compounds **228_{a-e}**-**233_{a-e}** were confirmed by their elemental analysis and spectral data (cf. experimental section). Compounds **228_{a-e}** clearly follow from disappearance of the NH₂ and NH bands in the IR and ¹H-NMR spectra and the appearance of the expected side chain signals in the ¹H-NMR spectra of compounds **229_{a-e}**-**232_{a-e}** (for more details cf. experimental section).

Interaction of compounds **218_{a-e}** with nitrous acid gave the corresponding 5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (**226_{a-e}**). The structures **226_{a-e}** clearly follow from disappearance the amino group bands in the IR spectra.

Triazines are used as cardiotoxic agents,⁸³ fungicide,⁷³ herbicides,⁸¹ blood platelet antiaggregation,⁸² antipsychotic agent,⁷⁷ and antimicrobial activity.⁸⁰ This high biological and pharmacological important of triazines and fused triazino heterocycles prompted us to synthesize 5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (**234_{a-e}**).

The chlorine atom reactivity at C-4 of compounds **226_{a-e}** was highlighted by its easy displacement with nucleophilic reagents as hydrazine hydrate to give the hydrazino derivatives **234_{a-e}** which in turn, proved to be a useful intermediate (Scheme 53).

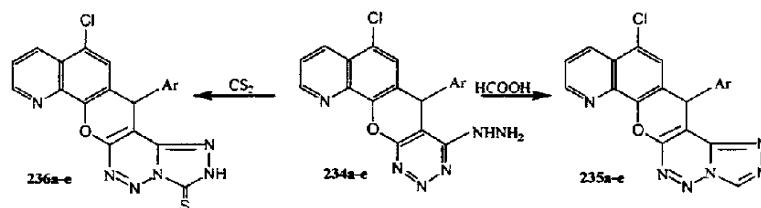


Scheme 53

The structures of compounds **234_{a-e}** were confirmed by elemental analysis, IR and ¹H-NMR spectra. The IR (KBr, ν cm⁻¹) spectrum of compound **234_a** showed absorption bands at 3473 (NH), 3324-3181 (NH₂). The ¹H-NMR (CDCl₃, δ ppm) showed the following signals: 4.30 (2H, s, NH₂), 5.00 (1H, s, pyran ring), 7.00-8.60 (9H, m, arom.) and 8.90 (1H, s, NH).

In fact, 14-aryl-12-chloro[1,2,4]triazolo[3",4"-f][1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (**235_{a-e}**) and 14-aryl-12-chloro-3-thioxo[1,2,4]triazolo[3",4"-f][1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (**236_{a-e}**) were produced from the reaction of

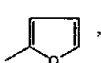
compounds **234_{a-e}** with formic acid and carbon disulfide respectively (cf. experimental section).



Ar = a) C_6H_5 ,

b) $\text{p-OCH}_3\text{C}_6\text{H}_4$,

c) $\text{p-NO}_2\text{C}_6\text{H}_4$,

d) ,

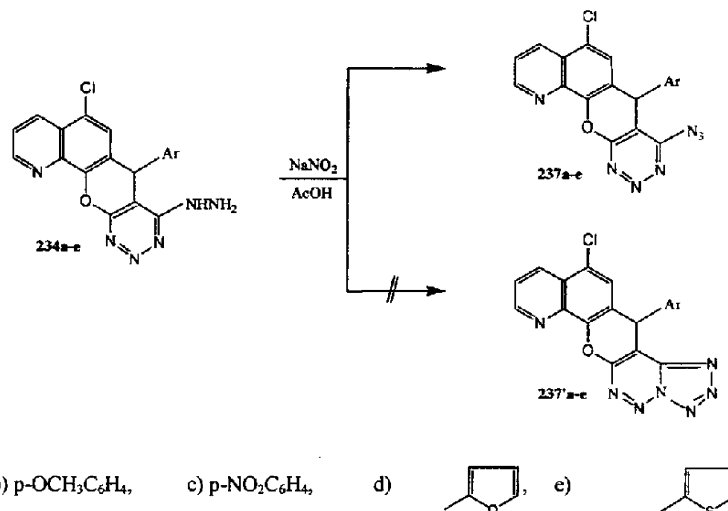
e) 

Scheme 54

The formation of compounds **235_{a-e}** - **236_{a-e}** were clearly obvious by the examination of their IR spectrum which revealed the absence of NH_2 and NH bands in compounds **235_{a-e}** and the presence of NH and CS bands in compounds **236_{a-e}**. The $^1\text{H-NMR}$ (CDCl_3 , δ ppm) of compound **235_a** and **236_a** (CF_3COOD , δ ppm) showed the following signals: 5.00 (1H, s, pyran ring), 6.60 (1H, s, triazolo), 7.10-8.60 (9H, m, arom.) and 5.00 (1H, s, pyran ring), 7.00-8.50 (9H, m, arom.) respectively.

In addition, treatment of **234_{a-e}** in acetic acid and an aqueous solution of sodium nitrite at room temperature gave one of the two structures showed in (Scheme 55).

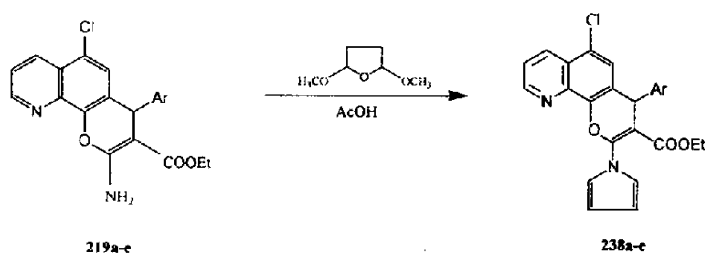
One of them is in agreement with the IR spectrum which revealed the appearance of a band characteristic to the azido group, so, this structure is 5-aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (**237_{a-e}**) and ruling out the alternative tetrazolo structures **237'_{a-e}** (Scheme 55).



Scheme 55

Recent years have witnessed the synthesis and characterization of a number of nitrogen-containing hetero aromatics. In fact, the biological activities of these compounds have drawn the attention of organic chemist for a long time. The synthesis of pyranoquinoline derivatives has gained very important goals to be used as antimicrobial activity.^{120, 134, 138-140} The pyrrolopyrazine derivatives were reported by Robba and his colleagues.¹⁴¹⁻¹⁴⁵ We presently involved in a program directed to the synthesis of pyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h]quinoline derivatives and related hexacyclic heterocycles.

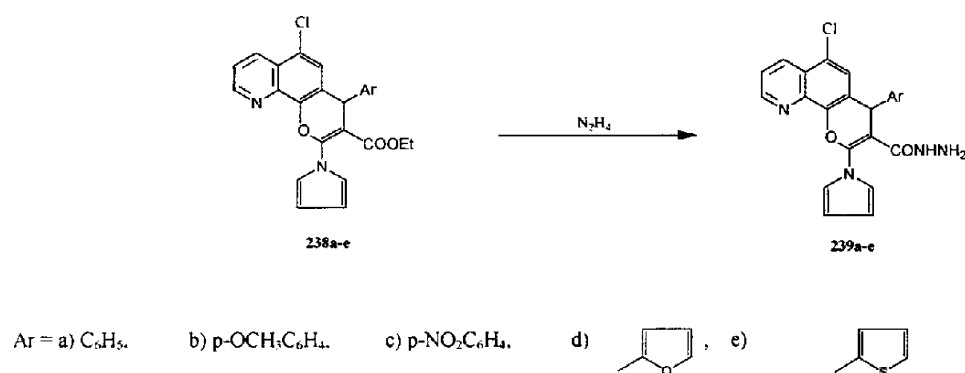
The amino function of ethyl 2-amino-4-aryl-6-chloro-4*H*-pyrano[3,2-h]quinoline-3-carboxylates (**219a-e**) were easily converted to the corresponding 1-pyrrolyl group via the interaction with 2,5-dimethoxytetrahydro furan in boiling acetic acid to give ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4*H*-pyrano[3,2-h]quinoline-3-carboxylates (**238a-e**) (Scheme 56).



Scheme 56

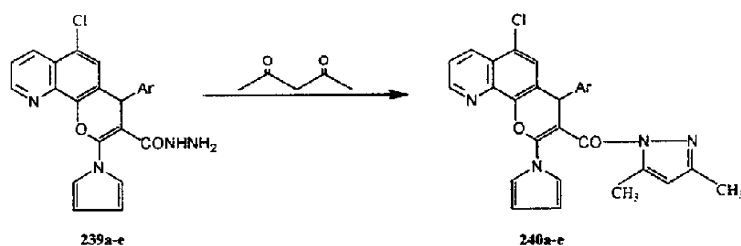
The structures of compounds **238_{a-e}** were conformed by elemental analysis and spectral data. The IR (KBr, ν cm^{-1}) showed the disappearance of the amino group band due to the formation of pyrrolyl ring. The $^1\text{H-NMR}$ (CDCl_3 , δ ppm) showed a new signals at 6.40-6.75 ppm which is assigned to the pyrrolyl-H atoms. For instance for compound **238_a**: 1.38 (3H, t, CH_3), 4.30 (2H, q, CH_2), 5.10 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.75 (2H, m, pyrrolyl ring), 7.10-8.60 (9H, m, arom.).

The latter pyrrolyl ester was reacted with hydrazine hydrate to give the pyrrolyl hydrazide **239_{a-e}** which indicated by the appearance of characteristic band of hydrazide group on its IR spectrum. The $^1\text{H-NMR}$ (CF_3COOD , δ ppm) of compound **239_a** showed the following signals: 5.00 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.70 (2H, m, pyrrolyl ring), 7.10-8.60 (9H, m, arom.) (Scheme 57).



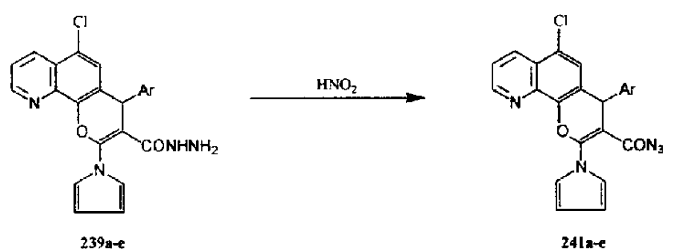
Scheme 57

2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano-[3,2-h]quinolines (**240_{a-e}**) were the product of the reaction between the hydrazides **239_{a-e}** and acetylacetone. The IR (KBr, ν cm^{-1}) spectrum **240_a** showed characteristic bands at 1700 cm^{-1} due to CO and at 1603 cm^{-1} due to C=N. The $^1\text{H-NMR}$ (CDCl_3 , δ ppm) spectrum of **240_a** showed the expected signal pattern at: 1.80 (6H, s, 2CH_3), 5.00 (1H, s, pyran ring), 6.30 (2H, m, pyrrolyl ring), 6.50 (2H, m, pyrrolyl ring), 7.10-8.50 (9H, m, arom.) (Scheme 58).



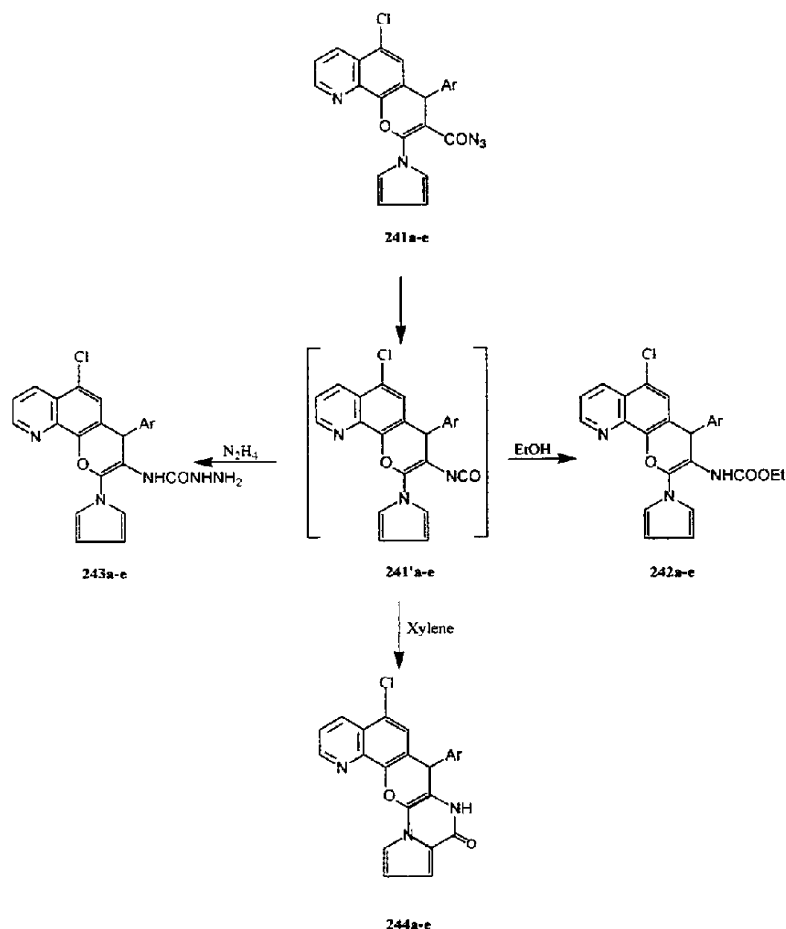
Scheme 58

The treatment of the hydrazide **239a-e** with nitrous acid gave the corresponding 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-yl azides (**241a-e**). The structure of compound **241a** was established by IR (appearance of a new band at 2213 cm⁻¹ due to the azide group) and ¹H-NMR spectra which showed the expected signals at: 5.10 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.60 (2H, m, pyrrolyl ring), 7.30-8.60 (9H, m, arom.) (cf. the experimental section).



Scheme 59


The acid azide is a versatile compound and could be transformed into a variety of derivatives. When **241a-e** were heated in boiling ethanol, the ethylcarbamate **242a-e** were obtained. When they reacted with hydrazine hydrate, the products were the semicarbazides **243a-e** (Scheme 60).



Ar = a) C_6H_5 ,

b) $\text{p-OCH}_3\text{C}_6\text{H}_4$,

c) $\text{p-NO}_2\text{C}_6\text{H}_4$,

d) ,

e) 

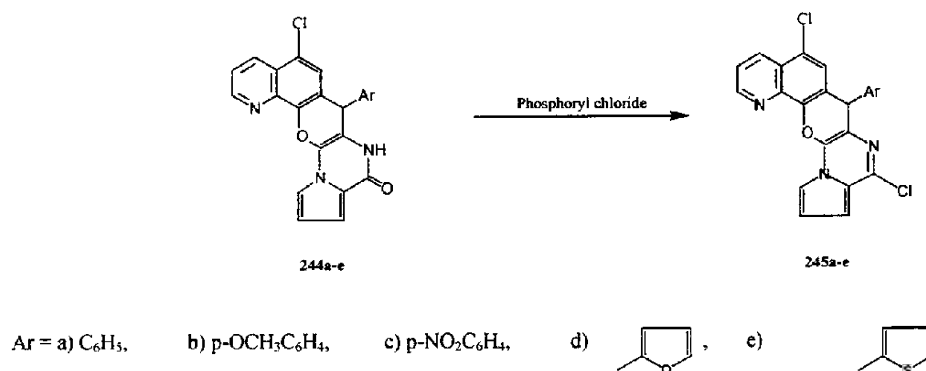
Scheme 60

The structures of compounds **242a-e** - **243a-e** were confirmed by their analytical and spectral data. The IR ((KBr, $\nu \text{ cm}^{-1}$) spectrum showed characteristic bands at 3375 (NH), 1707 (CO) for compound **242a** and at 3447 (NH), 3350-3160 (NH₂), 1700 (CO) for compound **243a**. The $^1\text{H-NMR}$ (CF_3COOD) showed the following signals: 2.10 (3H, t, CH_3), 4.20 (2H, q, CH_2), 5.10 (1H, s, pyran ring), 6.30 (2H, m, pyrrolyl ring), 6.60 (2H, m, pyrrolyl ring), 7.30-8.50 (9H, m, arom.) for compound **242a** and at 5.10 (1H, s, pyran ring), 6.20-8.30 (13H, m, arom.) for compound **243a** respectively.

Heating the acid azides **241a-e** in a high-boiling point inert solvent such as xylene led to Curtius rearrangement with concomitant ring closure of the isocyanate intermediate **241'a-e** giving 7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1",2":1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinolines (**244a-e**). The formation of **244a-e** are due to the high reactivity of the isocyanate intermediate which could not be isolated under the

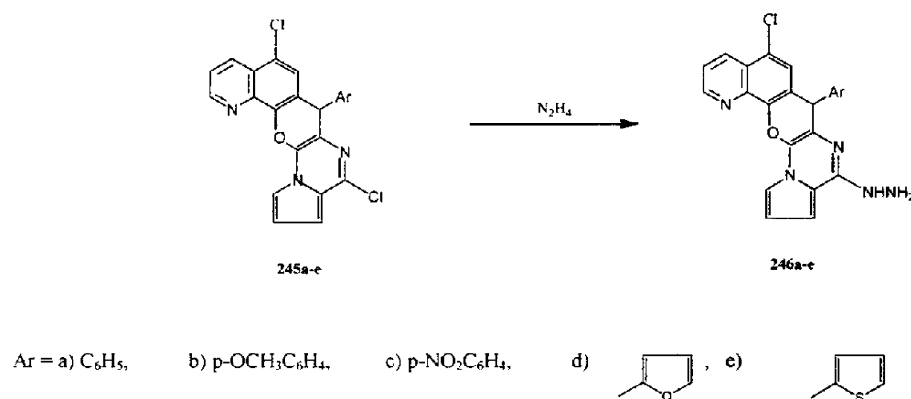
reaction conditions used. The structure of compound **244_a** was established by IR (absence of NH₂ band), Mass and ¹H-NMR spectra.

The latter oxo compounds **244_{a-e}** could be transformed into the corresponding chloro derivatives namely 7-Aryl-5,9-dichloropyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines (**245_{a-e}**) when heated under reflux with phosphoryl chloride. The structures **245_{a-e}** clearly follow from disappearance the NH bands in the IR and ¹H-NMR spectra and the appearance of the expected signals of the rest of the molecules in the ¹H-NMR spectra (Scheme 61).



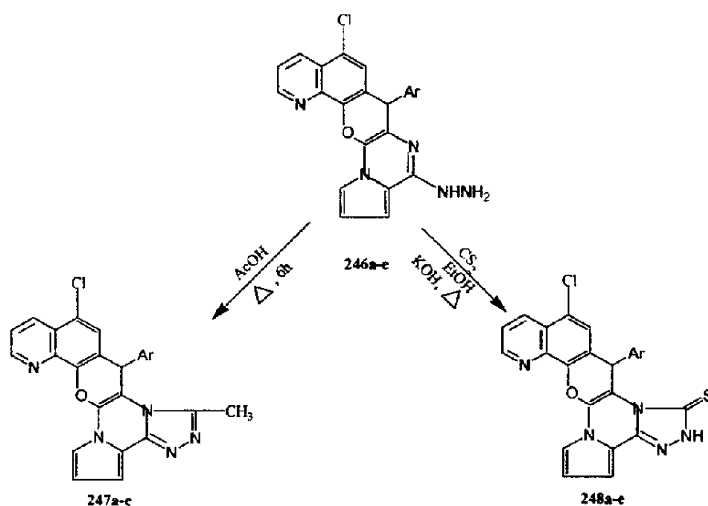
Scheme 61

The reactivity of the chlorine atom at C-9 of **245_{a-e}** was shown by its easy displacement using various nucleophilic reagents such as hydrazine hydrate to give 7-Aryl-5-chloro-9-hydrazinopyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines (**246_{a-e}**) (Scheme 62).



Scheme 62

The hydrazino derivatives **246_{a-e}** proved to be a useful compound for synthetics. The triazolo derivatives **247_{a-e}** and **248_{a-e}** were produced from the reaction of **246_{a-e}** with acetic acid and carbon disulfide respectively (Scheme 63).



Ar = a) C₆H₅,

b) p-OCH₃C₆H₄,

c) p-NO₂C₆H₄,

d) ,

e) 

Scheme 63

The structures of compounds **247_{a-e}** and **248_{a-e}** were confirmed by elemental analysis, IR, ¹H-NMR and MS spectroscopy. The IR ((KBr, ν cm⁻¹) spectrum of **247_a** showed the disappearance of NH band and the ¹H-NMR (CDCl₃, δ ppm) showed a new singlet at 2.10 ppm which is assigned to the methyl group.

Antibacterial Activity

The antibacterial activity of the synthesized compounds was tested against *Escherichia coli* and *Staphylococcus aureus* using the agar cup diffusion technique¹⁴⁶ and results of the biological testing are given in Table 1. The data showed that most of the newly synthesized compounds exhibited remarkable effects.

Antifungal activity

The newly synthesized compounds were screened for their antifungal activity against three species of fungi, namely, *Aspergillus flavus*, *Aspergillus niger* and *Penicillium chrysogenum*, using the disk diffusion method.¹⁴⁷⁻¹⁴⁸ The tested compounds were dissolved in N,N-dimethylformamide (DMF) to get a solution of 1% concentration. Filter paper discs (Whatman, 5 mm diameter) were saturated with this former solution. The saturated filter paper discs were placed on the surface of solidified Czapek's Dox agar dishes seeded by the test fungi. The inhibition zones were measured in mm at the end of an incubation period of 48h at 28 °C and 8-quinolinol was used as standard reference. As appear in Table 2, compounds **238_{a-c}**, **239_a**, **240_{a-c}**, **241_a**, **241_c**, **243_{a-b}**, **244_{a-b}**, **245_{a-c}**, **246_c** and **248_{a-c}** exhibited strong activity (inhibition zones ranged from 25-40 mm). Compounds **238_{d-e}**, **239_{b-c}**, **240_{d-e}**, **241_b**, **242_{a-b}**, **243_{c-e}**, **244_c**, **245_{d-e}**, **246_{a-b}**, **246_{d-e}** showed moderate activity (inhibition zones ranging from 11-20 mm). On the other hand, compounds **239_{d-e}**, **241_{d-e}**, **242_{c-e}**, **244_{d-e}**, **247_{a-c}** and **248_{d-e}** showed weak activity (inhibition zones ranged from 3-9 mm) in comparison to the standard.

Table1: Antimicrobial screening of compounds (218_{a-e}–236_{a-e}) (inhibition zones mm)

Compd. No.	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>	Compd. No.	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>
218a	22	16	224e	25	33
b	28	23	225a	31	32
c	21	19	b	24	35
d	33	22	c	21	15
e	44	27	d	23	20
220a	23	26	e	31	19
b	28	31	226a	20	21
c	-	19	b	26	17
d	23	19	c	-	28
e	36	22	d	19	21
221a	22	18	e	26	32
b	18	25	227a	20	29
c	21	21	b	33	35
d	16	16	c	19	-
e	29	34	d	17	21
222a	20	-	e	36	50
b	19	21	228a	22	31
c	23	18	b	37	27
d	-	18	c	26	19
e	19	-	d	23	28
223a	18	18	e	42	57
b	26	26	229a	18	21
c	-	-	b	23	19
d	19	19	c	18	24
e	36	29	d	-	16
224a	22	24	e	22	-
b	21	23	230a	24	33
c	23	15	b	40	29
d	21	19	c	14	22

Table 1 (contin.)

230d	27	31	233e	33	39
e	44	61	234a	21	25
231a	19	21	b	36	22
b	25	19	c	22	32
c	23	-	d	25	23
d	26	23	e	31	28
e	24	31	235a	-	21
232a	277	36	b	29	-
b	43	32	c	-	19
c	25	16	d	18	-
d	31	34	e	24	21
e	47	29	236a	31	36
233a	22	26	b	45	31
b	35	24	c	30	38
c	-	29	d	44	32
d	22	25	e	39	46
Tetracycline	12	15	Tetracycline	12	15

Table 2: Antifungal activity of tricyclic heterocyclic quinoline derivatives (238_{a-e}-248_{a-e}).

Inhibition of spore germination							
Compd. No.	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>	<i>Penicillium chrysogenum</i>	Compd. No.	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>	<i>Penicillium chrysogenum</i>
238a	25	32	23	243d	17	15	16
b	30	24	26	e	18	15	13
c	29	27	22	244a	40	36	31
d	14	17	15	b	36	28	37
e	12	15	13	c	19	13	15
239a	33	28	26	d	8	7	6
b	11	14	14	e	6	4	8
c	13	16	14	245a	35	31	26
d	6	4	10	b	29	23	21
e	9	6	8	c	31	28	25
240a	26	31	22	d	15	17	20
b	29	25	27	e	12	13	11
c	31	29	24	246a	14	11	14
d	15	18	16	b	13	16	18
e	14	16	13	c	34	28	31
241a	28	24	33	d	11	14	12
b	17	15	13	e	13	12	10
c	25	21	26	247a	8	5	6
d	8	6	9	b	8	8	6
e	9	8	11	c	7	9	10
242a	13	16	18	d	5	6	5
b	17	12	14	e	9	4	7
c	9	7	11	248a	38	40	33
d	6	8	4	b	31	36	26
e	3	5	6	c	34	27	29
243a	33	29	26	d	9	10	11
b	27	24	31	e	6	8	4
c	14	19	17	8-quinolinol	9	10	12

Experimental

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The time required for completion of each reaction was monitored by TLC. IR (v.cm^{-1}) spectra were recorded on a Nicolet Jeol technique in the range of $4000\text{--}400\text{ cm}^{-1}$ FTIR with KBr. $^1\text{H-NMR}$ (δ , ppm) spectra were recorded on an EM-360 90-MHz spectrometer using TMS as internal standard. $^{13}\text{C-NMR}$ (δ , ppm) were measured on a varian FT-80 spectrophotometer. Elemental analysis was determined on a Perkin Elmer 240 C microanalyser. Mass spectra were recorded on Jeol JMS 600 instrument (Assiut university).

2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines (218_{a-c}).

General procedure: A mixture of arylidenemalononitrile (0.01 mol) and 5-chloro-8-quinolinol (**217**) (0.01 mol) was heated under reflux in absolute ethanol (50 ml) using a catalytic amount of piperidine for 6h. The solvent was evaporated under reduced pressure, cooled and poured into ice cold water. The solid products were collected, washed several times with water and recrystallized from ethanol.

a: Yellowish brown crystals (68% yield), mp. 123 °C.

Analysis of $\text{C}_{19}\text{H}_{12}\text{N}_3\text{OCl}$ (333.82). Calcd. %: C, 68.36; H, 3.62; N, 12.59; Cl, 10.64; Found %: C, 68.47; H, 3.69; N, 12.48; Cl, 10.70

IR: 2192 (CN), 3324-3180 (NH_2), 3057 (CH arom.), 2924-2858 (CH aliph.) (fig.2). MS, m/z: 333.76 (fig.3).

$^1\text{H-NMR}$ (CDCl_3): 4.90 (1H,s), 8.8 (2H,s), 6.90-8.10 (9H,m). (fig.3)

$^{13}\text{C-NMR}$: 158.86, 148.34, 133.44, 129.18, 127.44, 126.81, 122.56, 115.09, 111.79, 92.13, 77.30, 76.67, 55.77.

b: Pale yellow crystals (73% yield), mp. 73 °C.

Analysis of $\text{C}_{20}\text{H}_{14}\text{N}_3\text{O}_2\text{Cl}$ (363.84). Calcd. %: C, 66.02; H, 3.88; N, 11.55; Cl, 9.76. Found %: C, 66.17; H, 3.91; N, 11.64; Cl, 9.81.

IR: 2192 (CN), 3390-3190 (NH_2), 2837 (CH aliph.) (fig.4). MS, m/z: 363.60

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 3.20 (3H, s), 6.90-8.10 (8H, m), 8.15 (2H, s).

c: Pale brown crystals (77% yields), mp. 82 °C.

Analysis of $C_{19}H_{11}N_4O_3Cl$ (378.82). Calcd. %: C, 60.24; H, 2.93; N, 14.79; Cl, 9.37. Found %: C, 60.37; H, 2.89; N, 14.66; Cl, 9.44.

IR: 2182 (CN), 3318-3062 (NH_2) (fig.6). MS, m/z: 378.81 (fig.7).

1H -NMR ($CDCl_3$): 4.90 (1H, s), 6.90-8.10 (8H, m), 8.15 (2H, s) (fig.7).

d: Dark brown crystals (85% yields), mp. 117 °C.

Analysis of $C_{17}H_{10}N_3O_2Cl$ (323.78). Calcd. %: C, 63.06; H, 3.11; N, 12.98; Cl, 10.96. Found %: C, 63.22; H, 3.16; N, 12.20; Cl, 10.84.

IR: 2217 (CN), 3324-3196 (NH_2). MS, m/z: 323.84 (fig. 8).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.70-8.00 (7H, m), 8.10 (2H, s).

e: Dark brown crystals (82% yields), mp. 111 °C.

Analysis of $C_{17}H_{10}N_3OSCl$ (339.88). Calcd. %: C, 60.07; H, 2.97; N, 12.37; S, 9.45; Cl, 10.45. Found %: C, 60.24; H, 2.89; N, 12.46; S, 9.54; Cl, 10.55.

IR: 2212 (CN), 3318-3196 (NH_2). MS, m/z: 339.97 (fig.9).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.70-8.00 (7H, m), 8.10 (2H, s).

Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate (219_{a-c}).

A mixture of cinnamionitrile derivatives (0.01 mol) and 5-chloro-8-quinolinol (**217**) (0.01 mol) was heated under reflux in absolute ethanol (50 ml) using a catalytic amount of piperidine for 6h. The solvent was evaporated under reduced pressure, cooled and the product was collected by filtration and recrystallized from methanol.

a: Brown crystal (65% yield), mp. 114 °C.

Analysis of $C_{21}H_{17}N_2O_3Cl$ (380.87). Calcd. %: C, 66.22; H, 4.50; N, 7.36; Cl, 9.32. Found %: C, 66.34; H, 4.46; N, 7.43; Cl, 9.26.

IR: 1731 (CO), 3472-3272 (NH_2) (fig.10). MS, m/z 380.97 (fig.11).

1H -NMR ($CDCl_3$): 5.10 (1H, s), 1.30 (3H, t), 4.20 (2H, q), 7.10-8.50 (9H, m), 8.90 (2H, s).

b: Pale yellow crystals (79% yield), mp. 101 °C.

Analysis of $C_{22}H_{19}N_2O_4Cl$ (410.89). calcd. %: C, 64.30; H, 4.66; N, 6.82; Cl, 8.64. Found %: C, 64.44; H, 4.73; N, 6.73; Cl, 8.71.

IR: 1716 (CO), 3324-3180 (NH_2) (fig.12).

$^1\text{H-NMR}$ (CDCl_3): 3.20 (3H, s), 1.35 (3H, t), 4.25 (2H, q), 5.10 (1H, s), 7.00-8.45 (8H, m), 8.90 (2H, s).

c: Pale brown crystals (72% yield), mp. 96 °C.

Analysis of $\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_5\text{Cl}$ (425.87). Calcd. %: C, 59.22; H, 3.79; N, 9.87; Cl, 8.34. Found %: C, 59.34; H, 3.73; N, 9.94; Cl, 8.28.

IR: 1700(CO), 3390-3242(NH_2) (fig.13).

$^1\text{H-NMR}$ (CF_3COOD): 5.10 (1H, s), 1.30 (3H, t), 4.15 (2H, q), 7.10-8.40 (8H, m).

d: Dark brown crystals (83% yield), mp. 119 °C.

Analysis of $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_4\text{Cl}$ (370.83). Calcd. %: C, 61.54; H, 4.08; N, 7.56; Cl, 9.57. Found %: C, 61.65; H, 4.16; N, 7.47; Cl, 9.46.

IR: 1711 (CO), 3360-3186 (NH_2) (fig.14).

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 1.35 (3H, t), 4.00 (2H, q), 6.80-7.90 (7H, m).

e: Orange crystals (80% yield), mp. 83 °C.

Analysis of $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_3\text{SCl}$ (386.93). Calcd. %: C, 58.98; H, 3.91; N, 7.24; S, 8.30; Cl, 9.18. Found %: C, 58.85; H, 3.83; N, 7.33; S, 8.22; Cl, 9.30.

IR: 1716 (CO), 3324-3196 (NH_2) (fig.15).

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 1.35 (3H, t), 4.00 (2H, q), 6.60-7.80 (7H, m).

7-Aryl-5-chloro-10-methyl-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]-pyrano[3,2-h]quinolines (220_{a-e}).

General procedure: A solution of **218_{a-e}** (0.01 mol) in acetic anhydride/pyridine mixture (20 ml, 2:1 v/v) was heated under reflux on a steam bath for 8h and poured into ice cold water. The products were collected, washed several times with water and recrystallized from dioxane.

a: Dark brown crystals (76% yield), mp. 170 °C.

Analysis of $\text{C}_{21}\text{H}_{14}\text{N}_3\text{O}_2\text{Cl}$ (375.85). Calcd. %: C, 67.10; H, 3.76; N, 11.18; Cl, 9.45. Found %: C, 67.23; H, 3.82; N, 11.26; Cl, 9.53.

IR: 1655 (CO), 3390 (NH) (fig.16). MS, m/z: 375.85 (fig.16).

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 3.40 (3H, s), 7.00-8.20 (9H, m).

b: Reddish brown crystals (78% yield), mp. 196 °C.

Analysis of $\text{C}_{22}\text{H}_{16}\text{N}_3\text{O}_3\text{Cl}$ (405.88). Calcd. %: C, 65.10; H, 3.97; N, 10.36;

Cl, 8.75. Found %: C, 65.26; H, 3.91; N, 10.28; Cl, 8.69.

IR: 3432 (NH), 2930-2832 (CH aliph.) (fig.17).

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 3.80 (3H, s), 3.40 (3H, s), 7.00-8.20 (8H, m).

c: Dark green crystals (80% yield), mp. 126 °C.

Analysis of $\text{C}_{21}\text{H}_{13}\text{N}_4\text{O}_4\text{Cl}$ (420.85). calcd. %: C, 59.93; H, 3.11; N, 13.32;

Cl, 8.44. Found %: C, 59.80; H, 3.19; N, 13.41; Cl, 8.51.

IR: 1710 (CO), 3273 (NH) (fig.18).

$^1\text{H-NMR}$ (CF_3COOD): 4.90 (1H, s), 3.80 (3H, s), 7.00-8.20 (8H,m).

d: Pale brown crystals (88% yield), mp. 130 °C.

Analysis of $\text{C}_{19}\text{H}_{12}\text{N}_3\text{O}_3\text{Cl}$ (365.82). Calcd. %: C, 62.38; H, 3.31; N, 11.49;

Cl, 9.70. Found %: C, 62.25; H, 2.35; N, 11.57; Cl, 9.62.

IR: 1696 (CO), 3421 (NH) (fig.19).

$^1\text{H-NMR}$ (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 6.70-8.15 (7H, m).

e: Dark brown crystals (85% yield), mp. 175 °C.

Analysis of $\text{C}_{19}\text{H}_{12}\text{N}_3\text{O}_2\text{SCl}$ (381.92). Calcd. %: C, 59.75; H, 3.17; N, 11.01;

S, 8.41; Cl, 9.30. Found %: C, 59.64; H, 3.12; N, 11.22; S, 8.47; Cl, 9.22.

IR: 1685 (CO), 3421 (NH) (fig.20).

$^1\text{H-NMR}$ (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 6.70-8.15 (7H, m).

8-Amino-7-aryl-5-chloro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (221_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol) and formamide (25 ml) was heated under reflux for 5h. The reaction mixture was allowed to cool and the product was collected and recrystallized from methanol.

- a: Dark brown crystals (65% yield), mp. 110 °C.
Analysis of C₂₀H₁₃N₄OCl (360.84). Calcd. %: C, 66.57; H, 3.63; N, 15.53; Cl, 9.84. Found %: C, 66.47; H, 3.70; N, 15.64; Cl, 9.78.
IR: 3440-3340 (NH₂), 3020 (CH arom.). MS, m/z: 360.83 (fig.21).
¹H-NMR (DMSO-d₆): 5.00 (1H, s), 8.25 (2H, s), 7.25-8.10 (10H, m) (fig.21).
- b: Brown crystals (69% yield), mp. 109 °C.
Analysis of C₂₁H₁₃N₄O₂Cl (390.87). Calcd. %: C, 64.53; H, 3.35; N, 14.34; Cl, 9.08. Found %: C, 64.44; H, 3.41; N, 14.42; Cl, 9.16.
IR: 3440-3340 (NH₂), 3020 (CH arom.).
¹H-NMR (DMSO-d₆): 3.60 (3H, s), 5.00 (1H, s), 7.25-8.10 (9H, m), 8.25 (2H, s).
- c: Reddish brown crystals (71% yield), mp. 135 °C.
Analysis of C₂₀H₁₂N₅O₃Cl (405.85). Calcd. %: C, 59.18; H, 2.98; N, 17.26; Cl, 8.75. Found %: C, 59.03; H, 2.95; N, 17.33; Cl, 8.81.
IR: 3420-3310 (NH₂), 3020 (CH arom.). MS, m/z: 405.79.
¹H-NMR (CF₃COOD): 4.9 (1H, s), 7.25-8.40 (9H, m).
- d: Brown crystals (78% yield), mp. > 300 °C.
Analysis of C₁₈H₁₁N₄O₂Cl (350.81). Calcd. %: C, 61.62; H, 3.16; N, 15.97; Cl, 10.12. Found %: C, 61.73; H, 3.24; N, 15.88; Cl, 10.22.
IR: 3440-3340 (NH₂), 3020 (CH arom.).
¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.70-8.00 (8H, m).
- e: Brown crystals (74% yield), mp. 116 °C.
Analysis of C₁₈H₁₁N₄OSCl (366.91). Calcd. %: C, 58.92; H, 3.12; N, 15.27; S, 8.75; Cl, 9.68. Found %: C, 58.83; H, 3.08; N, 15.35; S, 8.61; Cl, 9.60.
IR: 3440-3340 (NH₂), 3030 (CH arom.).

**7-Aryl-5-chloro-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]pyrano
[3,2-h]quinolines (222_{a-e}).**

General procedure: A mixture of **218_{a-e}** (0.01 mol), formic acid (7 ml) in formamide (25 ml) was heated under reflux for 4h. The reaction mixture was allowed to cool, poured into ice cold water and the product was collected and recrystallized from dioxane.

a: Pale brown crystals (63% yield), mp. 115 °C.

Analysis of C₂₀H₁₂N₃O₂Cl (361.83): Calcd. %: C, 66.39; H, 3.34; N, 11.62; Cl, 9.81. Found %: C, 66.50; H, 3.29; N, 11.54; Cl, 9.75.

IR: 3100 (NH), 1690 (CO). MS, m/z: 361.85 (fig.22).

¹H-NMR (CF₃COOD): 4.90 (1H, s), 7.15-8.20 (10H, m).

b: Reddish brown crystals (66% yield), mp. 88 °C.

Analysis of C₂₁H₁₄N₃O₃Cl (391.85). Calcd. %: C, 64.36; H, 3.60; N, 10.73; Cl, 9.06. Found %: C, 64.23; H, 3.54; N, 10.67; Cl, 9.14.

IR: 3100 (NH), 1700 (CO). MS, m/z: 391.78

¹H-NMR (CF₃COOD): 4.90 (1H, s), 3.50 (3H, s), 7.15-8.20 (9H, m).

c: Pale green crystals (69% yield), mp. 105 °C.

Analysis of C₂₀H₁₁N₄O₄Cl (406.83). Calcd. %: C, 59.04; H, 2.73; N, 13.78; Cl, 8.73. Found %: C, 59.16; H, 2.67; N, 13.84; Cl, 8.81.

IR: 3100 (NH), 1700 (CO). MS, m/z: 406.81.

¹H-NMR (CF₃COOD): 4.80 (1H, s), 7.15-8.20 (9H, m).

d: Brown crystals (74% yield), mp. 235 °C.

Analysis of C₁₈H₁₀N₃O₃Cl (351.79). Calcd. %: C, 61.45; H, 2.87; N, 11.95; Cl, 10.09. Found %: C, 61.56; H, 2.92; N, 11.89; Cl, 10.15.

IR: 3100 (NH), 1705 (CO), 3010 (CH arom.).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.60-7.80 (8H, m).

e: Yellowish brown crystals (68% yield). Calcd. %: C, 58.76; H, 2.74; N, 11.43;

S, 8.73; Cl, 9.65. Found %: C, 58.67; H, 2.62; N, 11.51; S, 8.79; Cl, 9.73.

4-Aryl-6-chloro-3-cyano-2-(ethoxymethylenamino)-4H-pyrano
[3,2-h]quinolines (223_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol) and triethyl orthoformate (3 ml) in acetic anhydride (15 ml) was heated under reflux for 2h. The solid product was collected and recrystallized from methanol.

a: Pale brown crystals (71% yield), mp. 247 °C.

Analysis of C₂₂H₁₆N₃O₂Cl (389.88). Calcd. %: C, 67.77; H, 4.14; N, 10.78; Cl, 9.11. Found %: C, 67.66; H, 4.22; N, 10.69; Cl, 9.21.

IR: 2208 (CN) (fig.23). MS, m/z: 389.88 (fig.24).

¹H-NMR (CDCl₃): 4.95 (1H, s), 1.65 (3H, t), 4.20 (2H, q), 7.20-8.30 (10H, m).

b: Brown crystals (61% yield), mp. 220 °C.

Analysis of C₂₃H₁₈N₃O₃Cl (419.90). Calcd. %: C, 65.79; H, 4.32; N, 10.01; Cl, 8.45. Found %: C, 65.66; H, 4.29; N, 10.12; Cl, 8.51.

IR: 2208 (CN), 2930 (CH aliph.) (fig.25). MS, m/z: 420.

¹H-NMR (CDCl₃): 4.95 (1H, s), 1.60 (3H, t), 3.80 (3H, s), 4.10 (2H, q), 7.20-8.30 (9H, m).

c: Pale brown crystals (64% yield), mp. 129 °C.

Analysis of C₂₂H₁₅N₄O₄Cl (434.88). Calcd. %: C, 60.76; H, 3.48; N, 12.89; Cl, 8.16. Found %: C, 60.85; H, 3.54; N, 12.97; Cl, 8.24.

IR: 2218 (CN), 2940 (CH aliph.) (fig.26). MS, m/z: 434.83.

¹H-NMR (CDCl₃): 4.95 (1H, s), 1.50 (3H, t), 4.30 (2H, q), 7.20-8.30 (9H, m), (fig.26).

¹³C-NMR: 158.85, 150.87, 148.30, 133.42, 129.28, 123.98, 115.09, 77.30, 72.66, 69.90, 63.66, 61.47, 55.76, 53.84, 40.74, 30.69.

d: Dark brown crystals (77% yield), mp. > 300 °C.

Analysis of C₂₀H₁₄N₃O₃Cl (379.84). Calcd. %: C, 63.24; H, 3.72; N, 11.07; Cl, 9.35. Found %: C, 63.14; H, 3.69; N, 11.14; Cl, 9.40.

IR: 2200 (CN), 2900 (CH aliph.), 3000 (CH arom.).

¹H-NMR (CDCl₃): 5.00 (1H, s), 1.60 (3H, t), 4.10 (2H, q), 6.60-7.80 (8H, m).

e: Dark brown crystals (73% yield), mp. 256 °C.

Analysis of $C_{20}H_{14}N_3O_2SCl$ (395.94). Calcd. %: C, 60.67; H, 3.56; N, 10.62; S, 8.11; Cl, 8.97. Found %: C, 60.56; H, 3.49; N, 10.73; S, 8.03; Cl, 8.86.
IR: 2218 (CN), 2919 (CH aliph.), 3078 (CH arom.) (fig.27).
 1H -NMR ($CDCl_3$): 5.00 (1H, s), 1.60 (3H, t), 4.10 (2H, q), 6.60-7.80 (8H, m).

7-Aryl-5-chloro-8-imino-9-phenyl-7H-pyrimido[4',5':6,5]pyrano-[3,2-h]quinolines (224_{a-e}).

General procedure: A mixture of **223_{a-e}** (0.01 mol) and aniline (0.01 mol) in absolute ethanol (50 ml) was refluxed for 3h. The precipitate was collected and recrystallized from ethanol.

a: Reddish brown crystals (58% yield), mp. 109 °C.

Analysis of $C_{26}H_{17}N_4OCl$ (436.94). Calcd. %: C, 71.47; H, 3.92; N, 12.83; Cl, 8.13. Found %: C, 71.57; H, 3.88; N, 12.91; Cl, 8.22.
IR: 3191 (NH) (fig.28). MS, m/z: 437.
 1H -NMR (CF_3COOD): 4.90 (1H, s), 7.10-8.20 (15H, m).

b: Pale yellow crystals (64% yield), mp. 251 °C.

Analysis of $C_{27}H_{19}N_4O_2Cl$ (466.96). Calcd. %: C, 69.44; H, 4.10; N, 12.00; Cl, 7.60. Found %: C, 69.32; H, 4.05; N, 12.10; Cl, 7.53.
IR: 3400 (NH), 2930 (CH aliph.) (fig.29). MS, m/z: 466.96 (fig.29).
 1H -NMR (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 7.10-8.20 (14H, m).

c: Pale brown crystals (61% yield), mp. 244 °C.

Analysis of $C_{26}H_{16}N_5O_3Cl$ (481.94). Calcd. %: C, 64.79; H, 3.35; N, 14.54; Cl, 7.37. Found %: C, 64.88; H, 4.40; N, 14.60; Cl, 7.44.
IR: 3319 (NH), 2935 (CH aliph.) (fig.30). MS, m/z: 482.
 1H -NMR (CF_3COOD): 4.90 (1H, s), 7.10-8.25 (14H, m).
 ^{13}C -NMR: 158.44, 148.33, 133.42, 129.16, 122.64, 114.42, 76.98, 72.66, 70.38, 63.66, 61.47, 55.76, 53.84, 40.47, 30.89.

d: Reddish brown crystals (71% yield), mp. 127 °C.

Analysis of $C_{24}H_{15}N_4O_2Cl$ (426.90). Calcd. %: C, 67.52; H, 3.54; N, 13.13; Cl, 8.32. Found %: C, 67.41; H, 3.61; N, 13.24; Cl, 8.26.
IR: 3319 (NH), 3058 (CH arom.) (fig.31).

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 6.60-7.80 (13H, m).

e: Pale brown crystals (66% yield), mp. 109 °C.

Analysis of $\text{C}_{24}\text{H}_{15}\text{N}_4\text{OSCl}$ (443). Calcd. %: C, 65.07; H, 3.41; N, 12.65; S, 7.25; Cl, 8.01. Found %: C, 65.19; H, 3.33; N, 12.54; S, 7.34; Cl, 8.12.

IR: 3334 (NH), 3026 (CH arom.) (fig.32). MS, m/z: 443.

$^1\text{H-NMR}$ (CF_3COOD): 5.00 (1H, s), 6.60-7.80 (13H, m).

8-Amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano-[3,2-h]quinolines (225_{a-e}).

General procedure: A mixture of 218_{a-e} (0.01 mol) and ethyl cyanoacetate (0.01 mol) was fused for 2h. the solid product was collected and recrystallized from dioxane.

a: Brown crystals (60% yield), mp. 155 °C.

Analysis of $\text{C}_{22}\text{H}_{13}\text{N}_4\text{O}_2\text{Cl}$ (400.86). Calcd. %: C, 65.91; H, 3.27; N, 13.98; Cl, 8.86. Found %: C, 65.82; H, 3.32; N, 13.92; Cl, 8.93.

IR: 3334-3201 (NH_2), 2203 (CN) (fig.33). MS, m/z: 400.84.

$^1\text{H-NMR}$ (CF_3COOD): 4.95 (1H, s), 7.00-8.10 (9H, m).

b: Pale brown crystals (61% yield), mp. 195 °C.

Analysis of $\text{C}_{23}\text{H}_{15}\text{N}_4\text{O}_3\text{Cl}$ (430.89). Calcd. %: C, 64.11; H, 3.51; N, 13.01; Cl, 8.24. Found %: C, 64.23; H, 3.46; N, 13.11; Cl, 8.31.

IR: 3329-3186 (NH_2), 2208 (CN) (fig.34).

$^1\text{H-NMR}$ (CF_3COOD): 4.95 (1H, s), 3.80 (3H, s), 7.00-8.10 (8H, m) (fig.34).

c: Pale brown crystals (68% yield), mp. 130 °C.

Analysis of $\text{C}_{22}\text{H}_{12}\text{N}_5\text{O}_4\text{Cl}$ (445.87). Calcd. %: C, 59.26; H, 2.71; N, 15.71; Cl, 7.96. Found %: C, 59.15; H, 2.78; N, 15.60; Cl, 7.87.

IR: 3191-3104 (NH_2), 3319 (NH), 2192 (CN), 2976 (CH arom.) (fig.35).

$^1\text{H-NMR}$ (CF_3COOD): 4.95 (1H, s), 7.00-8.10 (8H, m).

d: Brown crystals (72% yield), mp. 137 °C.

Analysis of $\text{C}_{20}\text{H}_{11}\text{N}_4\text{O}_3\text{Cl}$ (390.83). Calcd. %: C, 61.46; H, 2.84; N, 14.34; Cl, 9.08. Found %: C, 61.56; H, 2.80; N, 14.42; Cl, 9.17.

IR: 3319-3191 (NH₂), 2218 (CN) (fig.36).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.70-7.85 (7H, m).

e: Dark brown crystals (66% yield), mp. > 300 °C.

Analysis of C₂₀H₁₁N₄O₂SCl (406.93). Calcd. %: C, 59.03; H, 2.73; N, 13.77;

S, 7.89; Cl, 8.72. Found %: C, 59.13; H, 2.77; N, 13.84; S, 7.96; Cl, 8.67.

IR: 3191-3093 (NH₂), 3339 (NH), 2208 (CN) (fig.37).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.70-7.85 (7H, m).

5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (226_{a-e}).

General procedure: To an ice cold solution of **218_{a-e}** (0.01 mol) in a mixture of acetic acid (20 ml) and hydrochloric acid (10 ml), sodium nitrite (0.01 mol in 10 ml water) was added with stirring for 30 minutes and the stirring was continued for 3h. The product was collected and recrystallized from diluted acetic acid.

a: Yellowish brown crystals (64% yield), mp. 170 °C.

Analysis of C₁₉H₁₀N₄OCl₂ (381.31). Calcd. %: C, 59.84; H, 2.64; N, 14.70;

Cl, 18.62. Found %: C, 59.98; H, 2.71; N, 14.61; Cl, 18.51.

IR: 3000 (CH arom.).

¹H-NMR (CDCl₃): 4.90 (1H, s), 7.20-8.30 (9H, m).

b: Brown crystals (69% yield), mp. 114 °C.

Analysis of C₂₀H₁₂N₄O₂Cl₂ (411.34). Calcd. %: C, 58.40; H, 2.94; N, 13.62;

Cl, 17.26. Found %: C, 58.26; H, 2.90; N, 13.50; Cl, 17.32.

IR: 2945 (CH arom.) (fig.38). MS, m/z: 411.

¹H-NMR (CDCl₃): 3.20 (3H, s), 4.90 (1H, s), 7.20-8.30 (8H, m).

c: Pale brown crystals (58% yield), mp. 187 °C.

Analysis of C₁₉H₉N₅O₃Cl₂ (426.31). Calcd. %: C, 53.53; H, 2.13; N, 16.43;

Cl, 16.66. Found %: C, 53.62; H, 2.18; N, 16.54; Cl, 16.58.

IR: 3000 (CH arom.).

¹H-NMR (CDCl₃): 4.90 (1H, s), 7.20-8.30 (8H, m).

d: Dark brown crystals (55% yield), mp. 250 °C.

Analysis of $C_{17}H_8N_4O_2Cl_2$ (371.27). Calcd. %: C, 54.99; H, 2.17; N, 15.09; Cl, 19.12. Found %: C, 54.88; H, 2.22; N, 15.18; Cl, 19.05.

IR: 3083 (CH arom.) (fig.39).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.60-7.80 (7H, m).

e: Brown crystals (57% yield), mp. 200 °C.

Analysis of $C_{17}H_8N_4OSCl_2$ (387.37). Calcd. %: C, 52.71; H, 2.08; N, 14.47; S, 8.29; Cl, 18.33. Found %: C, 52.84; H, 2.15; N, 14.35; S, 8.38; Cl, 18.22.

IR: 3000 (CH arom.) (fig.40).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.60-7.80 (7H, m).

2-Amino-4-aryl-3-(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]-quinolines (227_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol), ethylenediamine (0.011 mol) and p-toluensulfonic acid monohydrate (0.012 mol) was heated under reflux for 12h. The reaction mixture was made alkaline with a saturated aqueous solution of sodium carbonate and the precipitate was filtered off and recrystallized from proper solvent.

a: Yellow crystals from methanol (62% yield), mp. 180 °C.

Analysis of $C_{21}H_{17}N_4OCl$ (376.89). Calcd. %: C, 66.92; H, 4.55; N, 14.87; Cl, 9.42. Found %: C, 66.78; H, 4.48; N, 14.95; Cl, 9.35.

IR: 3288-3037 (NH_2), 3437 (NH) (fig.41). MS, m/z: 376.81.

1H -NMR ($CDCl_3$): 4.95 (1H, s), 6.60 (2H, s), 8.95 (1H, s), 3.30 (2H, t), 3.90 (2H, t), 7.00-8.45 (9H, m) (fig.41).

b: Pale yellow crystals from dioxane (68% yield), mp. 161 °C.

Analysis of $C_{22}H_{19}N_4O_2Cl$ (406.91). Calcd. %: C, 64.93; H, 4.71; N, 13.77; Cl, 8.72. Found %: C, 64.85; H, 4.66; N, 13.85; Cl, 8.64.

IR: 3440-3340 (NH_2).

1H -NMR (CF_3COOD): 5.00 (1H, s), 3.35 (2H, t), 3.80 (2H, t), 3.30 (3H, s), 6.90-8.30 (8H, m).

c: Pale orange crystals from methanol (74% yield), mp. 148 °C.

Analysis of $C_{21}H_{16}N_5O_3Cl$ (421.89). Calcd. %: C, 59.78; H, 3.82; N, 16.60; Cl, 8.42. Found %: C, 59.87; H, 3.87; N, 16.54; Cl, 8.48.

IR: 3350-3211 (NH₂), 3452 (NH) (fig.42).

¹H-NMR (CDCl₃): 5.00 (1H, s), 3.40 (2H, t), 3.90 (2H, t), 6.70 (2H, s), 9.00 (1H, s), 7.00-8.40 (8H, m).

d: Brown crystals from ethanol (78% yield), mp. > 300 °C.

Analysis of C₁₉H₁₅N₄O₂Cl (366.850). Calcd. %: C, 62.20; H, 4.12; N, 15.28; Cl, 9.68. Found %: C, 62.31; H, 3.95; N, 15.19; Cl, 9.79.

IR: 3360-3159 (NH₂), 3432 (NH) (fig.43).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 3.40 (2H, t), 3.80 (2H, t), 7.00-8.30 (7H, m).

e: Pale brown crystals from dioxane (71% yield) mp. 206 °C.

Analysis of C₁₉H₁₅N₄OSCl (382.95). Calcd. %: C, 59.59; H, 3.95; N, 14.63; S, 8.38; Cl, 9.27. Found %: C, 59.47; H, 3.87; N, 14.71; S, 8.47; Cl, 9.36.

IR: 3216-3052 (NH₂), 3345 (NH) (fig.44).

¹H-NMR (CF₃COOD): 4.90 (1H, s), 3.40 (2H, t), 3.80 (2H, t), 7.00-8.40 (7H, m).

2,3,14-Trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (228_{a-e}).

General procedure: To a suspension of **227_{a-e}** (0.01 mol) in triethyl orthoformate (0.018 mol), was added small amount of formic acid (0.5 ml) and the mixture was heated under reflux for 7h. After cooling to rt, the product was collected by filtration and recrystallized from diluted acetic acid.

a: Pale yellow crystals from dioxane (58% yield) mp. 295 °C.

Analysis of C₂₂H₁₅N₄OCl (386.88). Calcd. %: C, 68.30; H, 3.91; N, 14.49; Cl, 9.18. Found %: C, 68.18; H, 3.85; N, 14.37; Cl, 9.25.

IR: 3058 (CH arom.) (fig.45). MS, m/z: 386.79.

¹H-NMR (CDCl₃): 4.95 (1H, s), 3.90-4.05 (4H, m), 7.10-8.50 (9H, m).

b: Yellow crystals from ethanol (65% yield), mp. 243 °C.

Analysis of C₂₃H₁₇N₄O₂Cl (416.91). Calcd. %: C, 66.26; H, 4.11; N, 13.44; Cl, 8.52. Found %: C, 66.39; H, 4.18; N, 13.57; Cl, 8.46.

IR: 3058 (CH arom.), 2930-2832 (CH aliph.) (fig.46).

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 3.40 (3H, s), 3.80-4.00 (4H, m),
7.00-8.40 (8H, m) (fig.46).

c: Pale brown crystals from ethanol (70% yield), mp. 257 °C.

Analysis of $\text{C}_{22}\text{H}_{14}\text{N}_5\text{O}_3\text{Cl}$ (431.88). Calcd. %: C, 61.18; H, 3.27; N, 16.22;
Cl, 8.22. Found %: C, 61.31; H, 3.31; N, 16.36; Cl, 8.31.

IR: 3037 (CH arom.), 2925-2848 (CH aliph.) (fig.47).

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 3.90-4.00 (4H, m), 7.00-8.35 (8H, m).

d: Brown crystals from ethanol (73% yield), mp. > 300 °C.

Analysis of $\text{C}_{20}\text{H}_{13}\text{N}_4\text{O}_2\text{Cl}$ (376.84). Calcd. %: C, 63.74; H, 3.48; N, 14.87;
Cl, 9.42. Found %: C, 63.85; H, 3.57; N, 14.96; Cl, 9.55.

IR: 3052 (CH arom.), 2937 (CH aliph.).

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 3.80-3.95 (4H, m), 6.85-8.10 (7H, m).

e: Brown crystals from methanol (67% yield), mp. 250 °C.

Analysis of $\text{C}_{20}\text{H}_{13}\text{N}_4\text{OSCl}$ (392.94). Calcd. %: C, 61.13; H, 3.34; N, 14.26;
S, 8.17; Cl, 9.04. Found %: C, 61.28; H, 3.41; N, 14.11; S, 8.26; Cl, 9.18.

IR: 3042 (CH arom.), 2930 (CH aliph.) (fig.48).

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 3.80-3.95 (4H, m) 6.80-8.00 (7H, m).

2,3,5,6,14-Pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (229_{a-e} – 232_{a-e}).

General procedure: To a solution of 227_{a-e} (0.01 mol) and the appropriate aldehyde (0.01 mol) or ketone (0.02 mol) in absolute ethanol (30 ml) was added concentrated hydrochloric acid (0.3 ml) and the mixture was stirred at 80-100 °C in a well stoppered round bottom flask fitted with reflux condenser for 12h. The product was isolated by column chromatography on silica gel with ethyl acetate/ methanol/ aq. Ammonia (6:2:2) as eluent.

229a: Dark brown crystals from methanol (35% yield), mp. > 300 °C.

Analysis of $\text{C}_{24}\text{H}_{19}\text{N}_4\text{OCl}$ (402.92). Calcd. %: C, 68.56; H, 4.75; N, 13.91;
Cl, 8.81. Found %: C, 68.45; H, 4.66; N, 13.80; Cl, 8.72.

$^1\text{H-NMR}$ (CDCl_3): 2.10 (3H, d), 3.50-3.90 (4H, m), 5.00 (1H, s),
2.8-3.0 (1H, q), 7.10-8.85 (9H, m) (fig.49).

- b: Brown crystals from dioxane (31% yield), mp. 224 °C.
 Analysis of $C_{24}H_{21}N_4O_2Cl$ (432.95). Calcd. %: C, 66.58; H, 4.89; N, 12.94; Cl, 8.20. Found %: C, 66.71; H, 4.78; N, 12.81; Cl, 8.31.
 IR: 2960-2919 (CH aliph.), 3400 (NH) (fig.50).
 1H -NMR ($CDCl_3$): 2.00 (3H, d), 2.20 (3H, s), 3.50-3.90 (4H, m), 5.00 (1H, s), 5.45 (1H, m), 6.60 (1H, s), 7.10-8.80 (8H, m).
- c: Brown crystals from ethanol (36% yield), mp. 242 °C.
 Analysis of $C_{23}H_{18}N_5O_3Cl$ (447.92). Calcd. %: C, 61.67; H, 4.05; N, 15.64; Cl, 7.93. Found %: C, 61.53; H, 4.13; N, 15.51; Cl, 7.85.
 1H -NMR ($CDCl_3$): 2.00 (3H, d), 3.50-3.80 (4H, m), 5.00 (1H, s), 5.50 (1H, m), 6.60 (1H, s), 7.10-8.80 (8H, m).
- d: Brown crystals from ethanol (39% yield), mp. > 300 °C.
 Analysis of $C_{21}H_{17}N_4O_2Cl$ (392.89). Calcd. %: C, 64.19; H, 4.36; N, 14.26; Cl, 9.04. Found %: C, 64.31; H, 4.43; N, 14.14; Cl, 9.13.
 1H -NMR ($CDCl_3$): 2.00 (3H, d), 3.35 (3H, s), 3.50-3.90 (4H, m), 5.00 (1H, s), 5.40 (1H, m), 6.50 (1H, s), 6.80-8.50 (7H, m).
- e: Brown crystals from dioxane (41% yield), mp. > 300 °C.
 Analysis of $C_{21}H_{17}N_4OSCl$ (408.99). Calcd. %: C, 61.67; H, 4.19; N, 13.70; S, 7.85; Cl, 8.68. Found %: C, 61.53; H, 4.25; N, 13.84; S, 7.71; Cl, 8.57.
 IR: 3400 (NH) (fig.51).
 1H -NMR ($CDCl_3$): 2.00 (3H, d), 3.50-3.80 (4H, m), 5.00 (1H, s), 5.50 (1H, m), 6.50 (1H, s), 6.70-8.60 (7H, m).
- 230a:** Pale brown crystals from ethanol, mp. > 300 °C.
 Analysis of $C_{24}H_{21}N_4OCl$ (416.95). Calcd. %: C, 69.13; H, 5.08; N, 13.44; Cl, 8.51. Found %: C, 69.29; H, 5.19; N, 13.56; Cl, 8.63.
 IR: 3359 (NH), 3063 (CH arom.), 2966 (CH aliph.) (fig.52).
 1H -NMR ($CDCl_3$): 2.90 (6H, s), 3.40-3.70 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (9H, m) (fig.52).
- b: Yellowish brown crystals from ethanol (34% yield), mp. > 300 °C.

Analysis of $C_{25}H_{23}N_4O_2Cl$ (446.97). Calcd. %: C, 67.18; H, 5.19; N, 12.54; Cl, 7.94. Found %: C, 67.32; H, 5.26; N, 12.41; Cl, 7.85.

IR: 3365 (NH), 3037 (CH arom.), 2930-2822 (CH aliph.) (fig.53).

1H -NMR ($CDCl_3$): 3.20 (3H, s), 2.90 (6H, s), 3.40-3.80 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.00-8.60 (8H, m).

c: Brown crystals from ethanol (34% yield), mp. > 300 °C.

Analysis of $C_{24}H_{20}N_5O_3Cl$ (461.95). Calcd. %: C, 62.40; H, 4.36; N, 15.16; Cl, 7.69. Found %: C, 62.29; H, 4.47; N, 15.05; Cl, 7.58.

IR: 3380 (NH), 2996-2868 (CH aliph.) (fig.54).

1H -NMR ($CDCl_3$): 2.90 (6H, s), 3.40-3.70 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (9H, m).

d: Greenish yellow crystals from dioxane (39% yield), mp. 290-292 °C.

Analysis of $C_{22}H_{19}N_4O_2Cl$ (406.91). Calcd. %: C, 64.93; H, 4.71; N, 13.77; Cl, 8.72. Found %: C, 64.78; H, 4.61; N, 13.63; Cl, 8.60.

IR: 3400 (NH), 2919 (CH aliph.) (fig.55).

1H -NMR ($CDCl_3$): 2.80 (6H, s), 3.40-3.75 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

e: Dark brown crystals from ethanol (32% yield), mp. 248 °C.

Analysis of $C_{22}H_{19}N_4OSCl$ (423.01). Calcd. %: C, 62.46; H, 4.53; N, 13.25; S, 7.59; Cl, 8.39. Found %: C, 62.59; H, 4.42; N, 13.38; S, 7.46; Cl, 8.26.

IR: 3400 (NH) (fig.56). MS, m/z: 423.

1H -NMR ($CDCl_3$): 2.80 (6H, s), 3.40-3.75 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.20 (7H, m).

231a: Pale brown crystals from methanol (58% yield), mp. 198 °C.

Analysis of $C_{26}H_{23}N_4OCl$ (442.98). Calcd. %: C, 70.49; H, 5.23; N, 12.65; Cl, 8.01. Found %: C, 70.38; H, 5.32; N, 12.76; Cl, 8.13.

IR: 3380 (NH), 2961-2863 (CH aliph.) (fig.57).

1H -NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.70-4.05 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 7.10-8.70 (9H, m).

b: Pale brown crystals from methanol (55% yield), mp. > 300 °C.

Analysis of $C_{27}H_{25}N_4O_2Cl$ (473.01). Calcd. %: C, 68.56; H, 5.33; N, 11.85; Cl, 7.51. Found %: C, 68.42; H, 5.41; N, 11.73; Cl, 7.69.

IR: 3365 (NH), 2945 (CH aliph.) (fig.58). MS, m/z: 473.

1H -NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.55 (3H, s), 3.70-4.50 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 7.00-8.60 (8H, m).

c: Brown crystals from ethanol (60% yield), mp. 250 °C.

Analysis of $C_{26}H_{22}N_5O_3Cl$ (487.99). Calcd. %: C, 63.99; H, 4.54; N, 14.36; Cl, 7.28. Found %: C, 63.84; H, 4.61; N, 14.45; Cl, 7.39.

IR: 3467 (NH), 3053 (CH arom.), 2925 (CH aliph.) (fig.59). MS, m/z: 488.

1H -NMR ($CDCl_3$): 1.50-1.90 (8H, m), 3.80-4.10 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.10-8.70 (8H, m) (fig.59).

d: Dark brown crystals from dioxane (56% yield), mp. > 300 °C.

Analysis of $C_{24}H_{21}N_4O_2Cl$ (432.95). Calcd. %: C, 66.58; H, 4.89; N, 12.94; Cl, 8.20. Found %: C, 66.42; H, 4.97; N, 12.79; Cl, 8.36.

IR: 3396 (NH), 2950 (CH aliph.) (fig.60).

1H -NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.70-4.00 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.40 (7H, m).

e: Brown crystals from dioxane (59% yield), mp. > 300 °C.

Analysis of $C_{24}H_{21}N_4OSCl$ (449.05). Calcd. %: C, 64.19; H, 4.71; N, 12.48; S, 7.15; Cl, 7.91. Found %: C, 64.36; H, 4.64; N, 12.33; S, 7.27; Cl, 7.82.

IR: 3406 (NH) 2945 (CH aliph.)(fig.61). MS, m/z: 449.

232a: Yellowish green crystals from methanol (56% yield), mp. > 300 °C.

Analysis of $C_{27}H_{25}N_4OCl$ (457.01). Calcd. %: C, 70.96; H, 5.51; N, 12.26; Cl, 7.77. Found %: C, 70.82; H, 5.43; N, 12.17; Cl, 7.84.

IR: 3421 (NH), 2935 (CH aliph.) (fig.62). MS, m/z: 457.

b: Yellow crystals from dioxane (59% yield), mp. > 300 °C.

Analysis of $C_{28}H_{27}N_4O_2Cl$ (487.04). Calcd. %: C, 69.05; H, 5.59; N, 11.51; Cl, 7.29. Found %: C, 69.18; H, 5.65; N, 11.38; Cl, 7.18.

IR: 3375 (NH), 2940 (CH aliph.) (fig.63).

¹H-NMR (CDCl₃): 1.40-1.80 (10H, m), 3.65 (3H, s), 3.90-4.10 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.10-8.50 (8H, m).

c: Pale brown crystals from methanol (60% yield), mp. 178 °C.

Analysis of C₂₇H₂₄N₅O₃Cl (502.01). Calcd. %: C, 64.59; H, 4.82; N, 13.95; Cl, 7.07. Found %: C, 64.43; H, 4.74; N, 13.80; Cl, 7.19.

IR: 3339 (NH), 2930-2858 (CH aliph.) (fig.64).

¹H-NMR (CDCl₃): 1.50-1.90 (10H, m), 3.90-4.10 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (8H, m).

d: Brown crystals from dioxane (63% yield), mp. > 300 °C.

Analysis of C₂₅H₂₃N₄O₂Cl (446.97). Calcd. %: C, 67.18; H, 5.19; N, 12.54; Cl, 7.94. Found %: C, 67.30; H, 5.28; N, 12.41; Cl, 7.82.

IR: 3391 (NH), 2930 (CH aliph.) (fig.65).

e: Dark brown crystals from dioxane (61% yield), mp. > 300 °C.

Analysis of C₂₅H₂₃N₄OSCl (463.07). Calcd. %: C, 64.84; H, 5.01; N, 12.10; S, 6.93; Cl, 7.67. Found %: C, 64.69; H, 5.12; N, 12.25; S, 6.81; Cl, 7.78.

IR: 3380 (NH) 2930 (CH aliph.)(fig.66).

¹H-NMR (CDCl₃): 1.50-1.80 (7H, m), 3.80-4.00 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 6.80-8.40 (7H, m).

5-Thioxo-2,3,6,14-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano-[3,2h]quinolines (233_{a-e}).

General procedure: A mixture of 227_{a-e} (0.01 mol), carbon disulfide (5 ml) in ethanol (50 ml) and two pellets of potassium hydroxide (0.17 g, 0.003 mol) was heated under reflux on water bath for 6h. the solid product obtained was dissolved in water and then acidified with acetic acid and recrystallized from diluted acetic acid.

a: Yellow crystals (63% yield), mp. > 300 °C.

Analysis of C₂₂H₁₅N₄OSCl (418.98). Calcd. %: C, 63.06; H, 3.61; N, 13.38; S, 7.66; Cl, 8.47. Found %: C, 63.17; H, 3.50; N, 13.25; S, 7.52; Cl, 8.35.

IR: 3432 (NH), 3058 (CH arom.) (fig.67).

¹H-NMR (CF₃COOD): 3.70-3.90 (4H, m), 4.90 (1H, s), 7.00-8.50 (9H, m).

b: Yellowish green crystals (61% yield), mp. 202 °C.

Analysis of $C_{23}H_{17}N_4O_2SCl$ (449.01). Calcd. %: C, 61.52; H, 3.82; N, 12.48; S, 7.15; Cl, 7.91. Found %: C, 61.64; H, 3.74; N, 12.33; S, 7.29; Cl, 7.75.
IR: 3375 (NH), 3058 (CH arom.), 2930-2822 (CH aliph.) (fig.68).
MS, m/z: 449.

c: Pale brown crystals (70% yield), mp. 122 °C.

Analysis of $C_{22}H_{14}N_5O_3SCl$ (463.98). Calcd. %: C, 56.95; H, 3.04; N, 15.10; S, 6.92; Cl, 7.65. Found %: C, 56.81; H, 3.15; N, 15.21; S, 6.79; Cl, 7.53.
IR: 3350 (NH), 3063 (CH arom.), 2920 (CH aliph.) (fig.69).
 1H -NMR (CF_3COOD): 3.80-4.00 (4H, m), 5.00 (1H, s), 7.10-8.60 (8H, m).

d: Dark brown crystals (70% yield), mp. 122 °C.

Analysis of $C_{20}H_{13}N_4O_2SCl$ (408.94). Calcd. %: C, 58.74; H, 3.20; N, 13.70; S, 7.85; Cl, 8.68. Found %: C, 56.58; H, 3.12; N, 13.83; S, 7.71; Cl, 8.53.
IR: 3391 (NH), 3053 (CH arom.), 2919 (CH aliph.) (fig.70).
 1H -NMR (CF_3COOD): 3.70-3.95 (4H, m), 5.00 (1H, s), 6.80-8.40 (7H, m).

e: Dark brown crystals (64% yield), mp. 225 °C.

Analysis of $C_{20}H_{13}N_4OS_2Cl$ (425.04). Calcd. %: C, 56.51; H, 3.08; N, 13.19; S, 7.55; Cl, 8.35. Found %: C, 56.66; H, 3.19; N, 13.05; S, 7.42; Cl, 8.23.
IR: 3400 (NH), 3053 (CH arom.) (fig.71).

5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines (234_{a-c}).

General procedure: A mixture of **226_{a-c}** (0.002 mol) and hydrazine hydrate (2 ml, 98%) in ethanol (30 ml) was heated under reflux for 6h. The product obtained after cooling was filtered off, washed with water and recrystallized from ethanol.

a: Yellow crystals (80% yield), mp. 199 °C.

Analysis of $C_{19}H_{13}N_6OCl$ (376.85). Calcd. %: C, 60.55; H, 3.48; N, 22.31; Cl, 9.42. Found %: C, 60.69; H, 3.57; N, 22.45; Cl, 9.56.
IR: 3324-3180 (NH_2), 3473 (NH), 3048 (CH arom.), 2935-2893 (CH aliph.) (fig.72).
 1H -NMR ($CDCl_3$): 4.30 (2H, s), 5.00 (1H, s), 7.00-8.60 (9H, m) (fig.72).

- b: Pale brown crystals (77% yield), mp. 195 °C.
 Analysis of $C_{20}H_{15}N_6O_2Cl$ (406.88). Calcd. %: C, 59.04; H, 3.72; N, 20.66; Cl, 8.73. Found %: C, 59.17; H, 3.81; N, 20.54; Cl, 8.60.
 IR: 3350-3201 (NH_2) (fig.73).
- c: Brown crystals (66% yield), mp. 148 °C.
 Analysis of $C_{19}H_{12}N_7O_3Cl$ (421.86). Calcd. %: C, 54.09; H, 2.87; N, 23.25; Cl, 8.42. Found %: C, 54.24; H, 2.94; N, 23.37; Cl, 8.51.
 IR: 3339-3206 (NH_2) (fig.74).
 1H -NMR ($CDCl_3$): 4.40 (2H, s), 5.00 (1H, s), 7.10-8.60 (8H, m), 8.95 (1H, s).
- d: Brown crystals (75% yield), mp. 147 °C.
 Analysis of $C_{17}H_{11}N_6O_2Cl$ (366.82). Calcd. %: C, 55.66; H, 3.02; N, 22.92; Cl, 9.68. Found %: C, 55.54; H, 2.94; N, 22.79; Cl, 9.56.
 IR: 3324-3201 (NH_2) (fig.75).
- e: Brown crystals (68% yield), mp. 260 °C.
 Analysis of $C_{17}H_{11}N_6OSCl$ (397.84). Calcd. %: C, 51.32; H, 2.79; N, 21.13; S, 8.07; Cl, 8.92. Found %: C, 51.47; H, 2.88; N, 21.28; S, 8.16; Cl, 8.79.
 1H -NMR ($CDCl_3$): 4.30 (2H, s), 5.00 (1H, s), 6.75-8.40 (7H, m), 8.80 (1H, s).

14-Aryl-12-chloro[1,2,4]triazolo[3'',4''-f][1,2,3]triazino[4',5':6,5]pyrano-[3,2-h]quinolines (235_{a-e}).

General procedure: A mixture of **234_{a-e}** (0.001 mol) in formic acid (20 ml) was heated under reflux for 8h. The reaction mixture was concentrated in vacuo and the solid product was collected, washed with water and recrystallized from methanol.

- a: Brown crystals (74% yield), mp. 178 °C.
 Analysis of $C_{20}H_{11}N_6OCl$ (386.85). Calcd. %: C, 62.09; H, 2.87; N, 21.73; Cl, 9.18. Found %: C, 62.21; H, 2.94; N, 21.62; Cl, 9.25.
 1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.60 (1H, s), 7.10-8.60 (9H, m) (fig.76).
- b: Brown crystals (68% yield), mp. 252 °C.
 Analysis of $C_{21}H_{13}N_6O_2Cl$ (416.87). Calcd. %: C, 60.50; H, 3.14; N, 20.17; Cl, 8.52. Found %: C, 60.35; H, 3.08; N, 20.29; Cl, 8.44.

$^1\text{H-NMR}$ (CDCl_3): 3.65 (3H, s), 5.00 (1H, s), 6.60 (1H, s), 7.00-8.40 (8H, m).

c: Dark brown crystals (61% yield), mp. > 300 °C.

Analysis of $\text{C}_{20}\text{H}_{10}\text{N}_7\text{O}_3\text{Cl}$ (431.85). Calcd. %: C, 55.62; H, 2.33; N, 22.71; Cl, 8.22. Found %: C, 55.49; H, 2.40; N, 22.60; Cl, 8.35.

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 6.60 (1H, s), 7.10-8.50 (8H, m).

d: Dark brown crystals (67% yield), mp. > 300 °C.

Analysis of $\text{C}_{18}\text{H}_9\text{N}_6\text{O}_2\text{Cl}$ (376.81). Calcd. %: C, 57.37; H, 2.41; N, 22.31; Cl, 9.42. Found %: C, 57.48; H, 2.52; N, 22.20; Cl, 9.31.

$^1\text{H-NMR}$ (CDCl_3): 4.90 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

e: Dark brown crystals (59% yield), mp. > 300 °C.

Analysis of $\text{C}_{18}\text{H}_9\text{N}_6\text{OSCl}$ (392.91). Calcd. %: C, 55.02; H, 2.31; N, 21.39; S, 8.17; Cl, 9.04. Found %: C, 55.15; H, 2.24; N, 21.26; S, 8.20; Cl, 9.17.

$^1\text{H-NMR}$ (CDCl_3): 4.90 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

14-Aryl-12-chloro-3-thioxo[1,2,4]triazolo[3'',4''-f][1,2,3]triazino-[4',5':6,5]pyrano[3,2-h]quinolines (236_{a-e}).

General procedure: A mixture of **234_{a-e}** (0.01 mol), carbon disulfide (5 ml) in ethanol (50 ml) and two pellets of potassium hydroxide was heated under reflux for 6h. The solid product obtained was dissolved in water and then acidified with acetic acid and recrystallized from diluted acetic acid.

a: Pale brown crystals (64% yield), mp. 168 °C.

Analysis of $\text{C}_{20}\text{H}_{11}\text{N}_6\text{OSCl}$ (418.95). Calcd. %: C, 57.33; H, 2.65; N, 20.07; S, 7.66; Cl, 8.47. Found %: C, 57.48; H, 2.74; N, 20.19; S, 7.52; Cl, 8.34.

IR: 3334 (NH), 1190 (CS) (fig.80).

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 6.80-8.10 (9H, m), 8.50 (1H, s).

b: Pale brown crystals (58% yield), mp. 195 °C.

Analysis of $\text{C}_{21}\text{H}_{13}\text{N}_6\text{O}_2\text{SCl}$ (448.97). Calcd. %: C, 56.18; H, 2.92; N, 18.72; S, 7.15; Cl, 7.91. Found %: C, 56.06; H, 2.84; N, 18.62; S, 7.26; Cl, 7.82.

IR: 3324 (NH) (fig.81).

$^1\text{H-NMR}$ (CF_3COOD): 3.50 (3H, s), 5.00 (1H, s), 7.10-8.40 (8H, m).

- c: Reddish brown crystals (56% yield), mp. 101 °C.
 Analysis of $C_{20}H_{10}N_7O_3SCl$ (463.95). Calcd. %: C, 51.77; H, 2.17; N, 21.14; S, 6.92; Cl, 7.52. Found %: C, 51.63; H, 2.25; N, 21.28; S, 6.81; Cl, 7.52.
 IR: 3350 (NH) (fig.82).
- d: Dark brown crystals (60% yield), mp. > 300 °C.
 Analysis of $C_{18}H_9N_6O_2SCl$ (408.91). Calcd. %: C, 52.87; H, 2.22; N, 20.56; S, 7.85; Cl, 8.68. Found %: C, 52.71; H, 2.31; N, 20.41; S, 7.70; Cl, 8.52.
 IR: 3206 (NH) (fig.83).
 1H -NMR (CF_3COOD): 5.00 (1H, s), 6.80-8.30 (7H, m).
- e: Brown crystals (54% yield), mp. 182 °C.
 Analysis of $C_{18}H_9N_6OS_2Cl$ (425.01). Calcd. %: C, 50.87; H, 2.14; N, 19.78; S, 15.11; Cl, 8.35. Found %: C, 50.92; H, 2.21; N, 19.66; S, 15.23; Cl, 8.23.
 IR: 3355 (NH) (fig.84). MS, m/z: 425.

5-Aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines (237_{a-c}).

General procedure: To a well-stirred solution of **234_{a-e}** (0.002 mol) in glacial acetic acid (50 ml), a solution of sodium nitrite (1 g in 10 ml of water) was added at rt and stirring was continued for 1h. The solid obtained was filtered off, washed with water and recrystallized from acetic acid.

- a: Brown crystals (61% yield), mp. 163 °C.
 Analysis of $C_{19}H_{10}N_7OCl$ (387.84). Calcd. %: C, 58.84; H, 2.60; N, 25.29; Cl, 9.15. Found %: C, 58.71; H, 2.50; N, 25.15; Cl, 9.26.
 IR: 2182 (N_3) (fig.85).
- b: Brown crystals (59% yield), mp. 185 °C.
 Analysis of $C_{20}H_{12}N_7O_2Cl$ (417.87). Calcd. %: C, 57.48; H, 2.90; N, 23.47; Cl, 8.50. Found %: C, 57.33; H, 2.83; N, 23.32; Cl, 8.41.
 IR: 2121 (N_3) (fig.86).
 1H -NMR ($CDCl_3$): 3.40 (3H, s), 5.00 (1H, s), 7.00-8.30 (8H, m) (fig.86).
- c: Brown crystals (55% yield), mp. 135 °C.

Analysis of $C_{19}H_9N_7O_3Cl$ (432.84). Calcd. %: C, 52.72; H, 2.10; N, 25.89; Cl, 8.20. Found %: C, 52.85; H, 2.17; N, 25.77; Cl, 8.07.
IR: 2182 (N_3) (fig.87).

d: Dark brown crystals (63% yield), mp. > 300 °C.

Analysis of $C_{17}H_8N_7O_2Cl$ (377.80). Calcd. %: C, 54.04; H, 2.14; N, 25.96; Cl, 9.40. Found %: C, 54.19; H, 2.05; N, 25.80; Cl, 9.27.
IR: 2126 (N_3) (fig.88).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.80-8.20 (7H, m).

e: Brown crystals (57% yield), mp. > 300 °C.

Analysis of $C_{17}H_8N_7OSCl$ (393.90). Calcd. %: C, 51.83; H, 2.05; N, 24.90; S, 8.15; Cl, 9.01. Found %: C, 51.66; H, 2.16; N, 24.74; S, 8.29; Cl, 9.16.
IR: 2126 (N_3) (fig.89).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.80-8.20 (7H, m).

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylates (238_{a-e}).

General procedure: A mixture of **219_{a-e}** (0.01 mol) and 2,5-dimethoxytetrahydrofuran (0.01 mol) in acetic acid (50 ml) was heated under reflux for 2h. After cooling, the precipitate formed was filtered off and recrystallized from ethanol.

a: Pale brown crystals (62% yield), mp. 126 °C.

Analysis of $C_{25}H_{19}N_2O_3Cl$ (430.92). Calcd. %: C, 69.68; H, 4.44; N, 6.50; Cl, 8.24. Found %: C, 69.82; H, 4.48; N, 6.41; Cl, 8.16.
IR: 1716 (CO) (fig.90). MS, m/z: 431 (fig.91).

1H -NMR ($CDCl_3$): 1.38 (3H, t), 4.30 (2H, q), 5.10 (1H, s), 6.40 (2H, m), 6.75 (2H, m), 7.10-8.60 (9H, m).

b: Brown crystals (71% yield), mp. 89 °C.

Analysis of $C_{26}H_{21}N_2O_4Cl$ (460.95). Calcd. %: C, 67.74; H, 4.59; N, 6.08; Cl, 7.70. Found %: C, 67.61; H, 4.51; N, 6.16; Cl, 7.83.
IR: 1701(CO) (fig.92).

1H -NMR ($CDCl_3$): 3.30 (3H, s), 1.35 (3H, t), 4.30 (2H, q), 5.00 (1H, s), 6.50 (2H, m), 6.80 (2H, m), 7.20-8.50 (8H, m) (fig.92).

- c: Pale brown crystals (65% yield), mp. 142 °C.
 Analysis of $C_{25}H_{18}N_3O_5Cl$ (475.92). Calcd. %: C, 63.09; H, 3.81; N, 8.83; Cl, 7.46. Found %: C, 63.20; H, 3.76; N, 8.78; Cl, 7.35.
 IR: 1710 (CO) (fig.93).
- d: Brown crystals (74% yield), mp. 176 °C.
 Analysis of $C_{23}H_{17}N_2O_4Cl$ (420.89). Calcd. %: C, 65.63; H, 4.07; N, 6.66; Cl, 8.44. Found %: C, 65.74; H, 4.12; N, 6.74; Cl, 8.35.
 IR: 1721(CO) (fig.94).
 1H -NMR ($CDCl_3$): 1.40 (3H, t), 4.30 (2H, q), 5.10 (1H, s), 6.40 (2H, m), 6.60 (2H, m), 6.80-8.20 (7H, m).
- e: Brown crystals (68% yield), mp. 98 °C.
 Analysis of $C_{23}H_{17}N_2O_3SCl$ (436.99). Calcd. %: C, 63.21; H, 3.92; N, 6.41; S, 7.35; Cl, 8.12. Found %: C, 63.33; H, 3.84; N, 6.31; S, 7.42; Cl, 8.21.
 IR: 1721(CO) (fig.95).

2-(1-pyrrolyl)-4aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbohydrazide (239_{a-e}).

General procedure: To a solution of the ester 238_{a-e} (0.01 mol) in hot ethanol (60 ml) was added an excess of hydrazine hydrate (5 ml, 98%) and the reaction mixture was refluxed for 5h. The solide product obtained was filtered off and recrystallized from diluted acetic acid.

- a: Yellowish brown crystals (65% yield), mp. 134 °C.
 Analysis of $C_{23}H_{17}N_4O_2Cl$ (416.91). Calcd. %: C, 66.26; H, 4.11; N, 13.44; Cl, 8.52. Found %: C, 66.15; H, 4.16; N, 13.50; Cl, 8.61.
 IR: 1700 (CO), 3324-3206 (NH_2), 3452 (NH) (fig.96). MS, m/z: 417 (fig.97).
 1H -NMR (CF_3COOD): 5.00 (1H, s), 6.40 (2H, m), 6.70 (2H, m), 7.10-8.60 (9H, m) (fig.97).
- b: Pale brown crystals (75% yield), mp. 151 °C.
 Analysis of $C_{24}H_{19}N_4O_3Cl$ (446.93). Calcd. %: C, 64.49; H, 4.29; N, 12.54; Cl, 7.94. Found %: C, 64.58; H, 4.34; N, 12.47; Cl, 7.85.
 IR: 1716 (CO), 3312-3202 (NH_2), 3450 (NH).

¹H-NMR (CF₃COOD): 3.40 (3H, s), 5.10 (1H, s), 6.40 (2H, m), 6.70 (2H, m), 7.10-8.40 (8H, m).

c: Yellowish brown crystals (69% yield), mp. 121 °C.

Analysis of C₂₃H₁₆N₅O₄Cl (461.91). Calcd. %: C, 59.80; H, 3.49; N, 15.17; Cl, 7.69. Found %: C, 59.95; H, 3.42; N, 15.23; Cl, 7.54.
IR: 1710 (CO), 3300-3200 (NH₂), 3450 (NH).

d: Pale brown crystals (78% yield), mp. 159 °C.

Analysis of C₂₁H₁₅N₄O₃Cl (406.87). Calcd. %: C, 61.99; H, 3.72; N, 13.77; Cl, 8.37. Found %: C, 61.86; H, 3.67; N, 13.69; Cl, 8.50.
IR: 1700 (CO), 3320-3215 (NH₂), 3435 (NH).
¹H-NMR (CF₃COOD): 5.10 (1H, s), 6.20 (2H, m), 6.60 (2H, m), 6.80-8.50 (7H, m).

e: Pale brown crystals (72% yield), mp. > 340 °C.

Analysis of C₂₁H₁₅N₄O₂SCl (422.97). Calcd. %: C, 59.63; H, 3.58; N, 13.25; S, 7.59; Cl, 8.39. Found %: C, 59.79; H, 3.62; N, 13.19; S, 7.68; Cl, 8.24.
IR: 1700 (CO), 3310-3200 (NH₂), 3420 (NH).

2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines (240_{a-e}).

General procedure: A mixture of **239_{a-e}** (0.01 mol) and excess of acetylacetone (10 ml) was refluxed for 5h. The excess acetylacetone was eliminated in vacuo and the solid product was collected and recrystallized from ethanol.

a: Brown crystals (61% yield), mp. 231 °C.

Analysis of C₂₈H₂₁N₄O₂Cl (481). Calcd. %: C, 69.91; H, 4.40; N, 11.65; Cl, 7.38. Found %: C, 69.79; H, 4.37; N, 11.72; Cl, 7.46.
IR: 1701(CO) (fig.98). MS, m/z: 481.44 (fig.99).
¹H-NMR (CDCl₃): 1.80 (6H, s), 5.00 (1H, s), 6.30 (2H, m), 6.55 (2H, m), 7.10-8.50 (9H, m) (fig.99).

b: Yellowish brown crystals (70% yield), mp. 173 °C.

Analysis of C₂₉H₂₃N₄O₂Cl (495.01). Calcd. %: C, 70.36; H, 4.68; N, 11.32; Cl, 7.17. Found %: C, 70.47; H, 4.74; N, 11.41; Cl, 7.28.

IR: 1706 (CO) (fig.100).

¹H-NMR (CDCl₃): 3.30 (3H, s), 5.10 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.20-8.50 (8H, m).

c: Pale brown crystals (65% yield), mp. 133 °C.

Analysis of C₂₈H₂₀N₅O₄Cl (526). Calcd. %: C, 63.93; H, 3.83; N, 13.32; Cl, 6.75. Found %: C, 63.83; H, 3.77; N, 13.24; Cl, 6.65.

IR: 1720 (CO).

d: Yellowish brown crystals (74% yield), mp. > 340 °C.

Analysis of C₂₆H₁₉N₄O₃Cl (470.95). Calcd. %: C, 66.30; H, 4.07; N, 11.90; Cl, 7.54. Found %: C, 66.42; H, 4.13; N, 11.81; Cl, 7.42.

IR: 1716 (CO).

¹H-NMR (CDCl₃): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.10-8.20 (7H, m).

e: Brown crystals (68% yield), mp. 112 °C.

Analysis of C₂₆H₁₉N₄O₂SCl (487.05). Calcd. %: C, 64.11; H, 3.93; N, 11.51; S, 6.59; Cl, 7.29. Found %: C, 64.22; H, 3.87; N, 11.43; S, 6.66; Cl, 7.18.

IR: 1722 (CO).

¹H-NMR (CDCl₃): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.20-8.40 (7H, m).

2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-oylazid (241_{a-c}).

General procedure: To a solution of **239_{a-c}** (0.01 mol) in glacial acetic acid (40 ml), a solution of sodium nitrite (0.01 mol in 10 ml water) was added at rt with stirring. Stirring was continued for 30 minutes and the precipitate was filtered off, washed with water and recrystallized from benzene.

a: Pale brown crystals (62% yield), mp. 185 °C.

Analysis of C₂₃H₁₄N₅O₂Cl (427.89). Calcd. %: C, 64.56; H, 3.30; N, 16.37; Cl, 8.30. Found %: C, 64.68; H, 3.38; N, 16.48; Cl, 8.19.

IR: 2213 (N₃), 1716 (CO) (fig.101). MS, m/z: 427.71 (fig.101).

b: Pale brown crystals (67% yield), mp. 108 °C.

Analysis of $C_{24}H_{16}N_5O_3Cl$ (457.92). Calcd. %: C, 62.95; H, 3.52; N, 15.30; Cl, 7.75. Found %: C, 62.82; H, 3.47; N, 15.43; Cl, 7.82.

IR: 2212 (N_3), 1705 (CO) (fig.102).

1H -NMR ($CDCl_3$): 3.50 (3H, s), 5.10 (1H, s), 6.40 (2H, m), 6.60 (2H, m), 7.30-8.50 (8H, m) (fig.102).

c: Pale brown crystals (61% yield), mp. 194 °C.

Analysis of $C_{23}H_{13}N_5O_4Cl$ (458.88). Calcd. %: C, 60.20; H, 2.86; N, 15.27; Cl, 7.74. Found %: C, 60.31; H, 2.94; N, 15.49; Cl, 7.81.

IR: 2210 (N_3), 1700 (CO).

d: Dark brown crystals (70% yield), mp. 338 °C.

Analysis of $C_{21}H_{12}N_5O_3Cl$ (417.86). Calcd. %: C, 60.36; H, 2.90; N, 16.76; Cl, 8.50. Found %: C, 60.48; H, 2.84; N, 16.88; Cl, 8.43.

IR: 2078 (N_3), 1706 (CO) (fig.103).

1H -NMR ($CDCl_3$): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 6.80-8.10 (7H, m).

e: Dark brown crystals (74% yield), mp. 257 °C.

Analysis of $C_{21}H_{12}N_5O_2SCl$ (433.96). Calcd. %: C, 58.12; H, 2.79; N, 16.14; S, 7.40; Cl, 8.18. Found %: C, 58.22; H, 2.87; N, 16.25; S, 7.51; Cl, 8.25.

IR: 2356 (N_3), 1680 (CO) (fig.104).

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbamate (241_{a-c}).

General procedure: Each compound of **241_{a-c}** (0.01 mol) was heated under reflux in excess of absolute ethanol (50 ml) for 2h. The reaction mixture was concentrated and left to cool. The solid product was recrystallized from ethanol.

a: Brown crystals (72% yield), mp. > 340 °C.

Analysis of $C_{25}H_{20}N_3O_3Cl$ (445.94). Calcd. %: C, 67.33; H, 4.52; N, 9.43; Cl, 7.96. Found %: C, 67.47; H, 4.58; N, 9.36; Cl, 8.04.

IR: 1707 (CO), 3375 (NH), (fig.105). MS, m/z: 446.02 (fig.106).

1H -NMR (CF_3COOD): 2.10 (3H, t), 4.20 (2H, q), 5.10 (1H, s), 6.30 (2H, m), 6.60 (2H, m), 7.30-8.50 (9H, m) (fig.106).

- b: Dark brown crystals (76% yield), mp. 192 °C.
 Analysis of $C_{26}H_{22}N_3O_4Cl$ (475.97). Calcd. %: C, 65.61; H, 4.66; N, 8.83; Cl, 7.46. Found %: C, 65.45; H, 5.58; N, 8.92; Cl, 7.62.
 IR: 1706 (CO), 3457 (NH) (fig.107).
- c: Brown crystals (70% yield), mp. > 340 °C.
 Analysis of $C_{25}H_{19}N_4O_5Cl$ (490.94). Calcd. %: C, 61.16; H, 3.90; N, 11.42; Cl, 7.23. Found %: C, 61.30; H, 3.78; N, 11.28; Cl, 7.34.
 IR: 1700 (CO), 3421 (NH) (fig.108).
 1H -NMR (CF_3COOD): 2.10 (3H, q), 4.10 (2H, q), 5.10 (1H, s), 6.30 (2H, m), 6.60 (2H, m), 7.20-8.50 (8H, m).
- d: Dark brown crystals (79% yield), mp. > 340 °C.
 Analysis of $C_{23}H_{18}N_3O_4Cl$ (435.90). Calcd. %: C, 63.37; H, 4.16; N, 9.64; Cl, 8.14. Found %: C, 63.22; H, 4.24; N, 9.75; Cl, 8.29.
 IR: 1706 (CO), 3406 (NH) (fig.109).
 1H -NMR (CF_3COOD): 2.20 (3H, t), 4.10 (2H, q), 6.20 (2H, m), 6.40 (2H, m), 7.00-8.30 (7H, m).
- e: Brown crystals (82% yield), mp. 285 °C.
 Analysis of $C_{23}H_{18}N_3O_3SCl$ (452). Calcd. %: C, 61.11; H, 4.01; N, 9.30; S, 7.10; Cl, 7.85. Found %: C, 61.24; H, 4.11; N, 9.21; S, 7.21; Cl, 7.93.
 1H -NMR (CF_3COOD): 2.20 (3H, t), 4.10 (2H, q), 6.20 (2H, m), 6.40 (2H, m), 7.00-8.30 (7H, m).

4-[2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-yl]semicarbazide (243_{a-e}).

General procedure: A mixture of 241_{a-e} (0.01 mol) and hydrazine hydrate (10 ml) was refluxed for 1h. On cooling the solid product was filtered off, washed with ethanol and recrystallized from ethanol.

- a: Brown crystals (70% yield), mp. 325 °C.
 Analysis of $C_{23}H_{18}N_5O_2Cl$ (431.92). Calcd. %: C, 63.95; H, 4.20; N, 16.22; Cl, 8.22. Found %: C, 63.81; H, 4.14; N, 16.15; Cl, 8.30.

IR: 3350-3160 (NH₂), 3446 (NH), 1690 (CO) (fig.110). MS, m/z: 432 (fig.110).

¹H-NMR (CF₃COOD): 5.10 (1H, s), 6.20-8.30 (13H, m).

b: Brown crystals (75% yield), mp. 246 °C.

Analysis of C₂₄H₂₀N₅O₃Cl (461.95). Calcd. %: C, 62.40; H, 4.36; N, 15.16; Cl, 7.69. Found %: C, 62.55; H, 4.42; N, 15.29; Cl, 7.78.

¹H-NMR (CF₃COOD): 3.20 (3H, s), 5.10 (1H, s), 6.25-8.30 (12H, m) (fig.111).

c: Dark brown crystals (69% yield), mp. 261 °C.

Analysis of C₂₃H₁₇N₆O₄Cl (476.93). Calcd. %: C, 57.92; H, 3.59; N, 17.63; Cl, 7.44. Found %: C, 57.79; H, 3.64; N, 17.74; Cl, 7.51.

IR: 3331-3230 (NH₂), 3440 (NH), 1690 (CO).

d: Dark brown crystals (78% yield), mp. > 340 °C.

Analysis of C₂₁H₁₆N₅O₃Cl (421.89). Calcd. %: C, 59.78; H, 3.82; N, 16.60; Cl, 8.42. Found %: C, 59.64; H, 3.76; N, 16.47; Cl, 8.51.

IR: 3300-3200 (NH₂), 3435 (NH), 1670 (CO).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.30-8.45 (11H, m).

e: Brown crystals (82% yield), mp. > 340 °C.

Analysis of C₂₁H₁₆N₅O₂SCl (437.99). Calcd. %: C, 57.58; H, 3.68; N, 15.99; S, 7.33; Cl, 8.11. Found %: C, 57.46; H, 3.73; N, 15.82; S, 7.44; Cl, 8.20.

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.30-8.40 (11H, m).

7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinolines (244_{a-e}).

General procedure: A solution of **241_{a-e}** (0.01 mol) in xylene (15 ml) was refluxed for one hour and then allowed to cool. The formed product was filtered off and recrystallized from ethanol.

a: Dark brown crystals (62% yield), mp. > 340 °C.

Analysis of C₂₃H₁₄N₃O₂Cl (399.87). Calcd. %: C, 69.08; H, 3.53; N, 10.51; Cl, 8.88. Found %: C, 69.20; H, 3.61; N, 10.62; Cl, 8.77.

IR: 3385 (NH), 1690 (CO) (fig.112). MS, m/z: 400.10 (fig.112).

¹H-NMR (CF₃COOD): 5.10 (1H, s), 6.45-8.25 (12H, m).

b: Brown crystals (65% yield), mp. 196 °C.

Analysis of C₂₄H₁₆N₃O₃Cl (429.90). Calcd. %: C, 67.05; H, 3.75; N, 9.78;

Cl, 8.26. Found %: C, 67.21; H, 3.82; N, 9.87; Cl, 8.32.

IR: 3391 (NH), 1690 (CO) (fig.113).

¹H-NMR (CF₃COOD): 3.30 (3H, s), 5.10 (1H, s), 6.40-8.30 (11H, m).

c: Brown crystals (61% yield), mp. > 340 °C.

Analysis of C₂₃H₁₃N₄O₄Cl (444.87). Calcd. %: C, 62.09; H, 2.95; N, 12.60;

Cl, 7.98. Found %: C, 62.23; H, 3.02; N, 12.74; Cl, 8.06.

IR: 3416 (NH), 1650 (CO) (fig.114).

¹H-NMR (CF₃COOD): 5.10 (1H, s), 6.40-8.30 (11H, m).

d: Dark brown crystals (66% yield), mp. > 340 °C.

Analysis of C₂₁H₁₂N₃O₃Cl (389.84). Calcd. %: C, 64.70; H, 3.10; N, 10.78;

Cl, 9.11. Found %: C, 64.55; H, 3.19; N, 10.86; Cl, 9.26.

IR: 3380 (NH), 1705 (CO) (fig.115).

e: Pale brown crystals (69% yield), mp. > 340 °C.

Analysis of C₂₁H₁₂N₃O₂SCl (405.94). Calcd. %: C, 62.13; H, 2.98; N, 10.35;

S, 7.91; Cl, 8.75. Found %: C, 62.26; H, 2.87; N, 10.44; S, 7.83; Cl, 8.82.

IR: 3380 (NH), 1664 (CO) (fig.116).

¹H-NMR (CF₃COOD): 5.00 (1H, s), 6.25-8.30 (10H, m).

7-Aryl-5,9-dichloropyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines (245_{a-e}).

General procedure: A suspension of 245_{a-e} (0.01 mol) in phosphoryl chloride (25 ml) was heated under reflux for 4h. The reaction mixture was poured into ice-water, the residual solid product was worked up in an ammonium hydroxide-ice mixture, filtered, washed with water and recrystallized from benzene.

a: Brown crystals (70% yield), mp. 254 °C.

Analysis of C₂₃H₁₃N₃OCl₂ (418.36). Calcd. %: C, 66.03; H, 3.13; N, 10.05;

Cl, 16.97. Found %: C, 66.17; H, 3.07; N, 10.14; Cl, 16.83.

$^1\text{H-NMR}$ (CDCl_3): 5.10 (1H, s), 6.35-8.40 (12H, m).

b: Brown crystals (73% yield), mp. 242 °C.

Analysis of $\text{C}_{24}\text{H}_{15}\text{N}_3\text{O}_2\text{Cl}_2$ (448.39). Calcd. %: C, 64.28; H, 3.37; N, 9.37; Cl, 15.83. Found %: C, 64.39; H, 3.43; N, 9.45; Cl, 15.72.

$^1\text{H-NMR}$ (CDCl_3): 3.30 (3H, s), 5.10 (1H, s), 6.30-8.40 (11H, m).

c: Dark brown crystals (68% yield), mp. 228 °C.

Analysis of $\text{C}_{23}\text{H}_{12}\text{N}_4\text{O}_3\text{Cl}_2$ (463.37). Calcd. %: C, 59.61; H, 2.61; N, 12.09; Cl, 15.32. Found %: C, 59.74; H, 2.56; N, 12.18; Cl, 15.20.

$^1\text{H-NMR}$ (CDCl_3): 5.10 (1H, s), 6.30-8.40 (11H, m).

d: Dark brown crystals (74% yield), mp. 298 °C.

Analysis of $\text{C}_{21}\text{H}_{11}\text{N}_3\text{O}_2\text{Cl}_2$ (408.33). Calcd. %: C, 61.77; H, 2.72; N, 10.29; Cl, 17.39. Found %: C, 61.64; H, 2.68; N, 10.18; Cl, 17.27.

$^1\text{H-NMR}$ (CDCl_3): 5.00 (1H, s), 6.25-8.30 (10H, m).

e: Brown crystals (77% yield), mp. 291 °C.

Analysis of $\text{C}_{21}\text{H}_{11}\text{N}_3\text{OSCl}_2$ (424.43). Calcd. %: C, 59.42; H, 2.61; N, 9.90; S, 7.56; Cl, 16.73. Found %: C, 59.31; H, 2.58; N, 9.82; S, 7.66; Cl, 16.60.

$^1\text{H-NMR}$ (CDCl_3): 5.10 (1H, s), 6.25-8.30 (10H, m).

7-Aryl-5-chloro-9-hydrazinopyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines (246_{a-e}).

General procedure: A mixture of **245_{a-e}** (0.01 mol) and hydrazine hydrate (5 ml, 98%) in ethanol (25 ml) was heated under reflux for 5h. The product formed after cooling was filtered, washed with ethanol and recrystallized from dioxane.

a: Dark brown crystals (64% yield), mp. 294 °C.

Analysis of $\text{C}_{23}\text{H}_{16}\text{N}_5\text{OCl}$ (413.91). Calcd. %: C, 66.74; H, 3.90; N, 16.92; Cl, 8.58. Found %: C, 66.62; H, 3.20; N, 16.99; Cl, 8.66.

IR: 3324-3181 (NH_2), 3473 (NH) (fig.117). MS, m/z: 414.02 (fig.117).

$^1\text{H-NMR}$ (CF_3COOD): 5.10 (1H, s), 6.30-8.20 (12H, m).

b: Dark brown crystals (66% yield), mp. 282 °C.

Analysis of $C_{24}H_{18}N_5O_2Cl$ (443.93). Calcd. %: C, 64.93; H, 4.09; N, 15.78; Cl, 8.00. Found %: C, 64.80; H, 4.15; N, 15.91; Cl, 7.89.
IR: 3300-3195 (NH_2), 3416 (NH).
 1H -NMR (CF_3COOD): 3.30 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m).

c: Brown crystals (62% yield), mp. 257 °C.

Analysis of $C_{23}H_{15}N_6O_3Cl$ (458.91). Calcd. %: C, 60.19; H, 3.30; N, 18.32; Cl, 7.74. Found %: C, 60.30; H, 3.41; N, 18.44; Cl, 7.81.
IR: 3315-3202 (NH_2), 3430 (NH).
 1H -NMR (CF_3COOD): 5.10 (1H, s), 6.30-8.30 (11H, m).

d: Dark brown crystals (68% yield), mp. > 340 °C.

Analysis of $C_{21}H_{14}N_5O_2Cl$ (403.87). Calcd. %: C, 62.45; H, 3.49; N, 17.35; Cl, 8.79. Found %: C, 62.57; H, 3.57; N, 17.47; Cl, 8.87.
IR: 3300-3180 (NH_2), 3446 (NH).

e: Brown crystals (71% yield), mp. 95 °C.

Analysis of $C_{21}H_{14}N_5OSCl$ (419.97). Calcd. %: C, 60.05; H, 3.36; N, 16.68; S, 7.64; Cl, 8.45. Found %: C, 60.15; H, 3.42; N, 16.81; S, 7.58; Cl, 8.38.
IR: 3310-3165 (NH_2), 3450 (NH).
 1H -NMR (CF_3COOD): 5.00 (1H, s), 6.20-8.25 (10H, m).

7-Aryl-5-chloro-9-methyl[1,2,4]triazolo[3'',4'':3',4']pyrrolo-[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines (247_{a-e}).

General procedure: A solution of **246_{a-e}** (0.01 mol) in acetic acid (30 ml) was heated under reflux for 6h. the reaction mixture was concentrated in vacuo and the solid product was collected, washed with water and recrystallized from acetic acid.

a: Brown crystals (55% yield), mp. 118°C.

Analysis of $C_{25}H_{16}N_5OCl$ (437.93). Calcd. %: C, 68.56; H, 3.68; N, 16.00; Cl, 8.11. Found %: C, 68.45; H, 3.73; N, 16.06; Cl, 8.19.
IR: 2925 (CH aliph.) (fig.118).
 1H -NMR ($CDCl_3$): 2.10 (3H, s), 5.10 (1H, s), 6.30-8.10 (12H, m).

b: Brown crystals (58% yield), mp. 234 °C.

Analysis of $C_{26}H_{18}N_5O_2Cl$ (467.95). Calcd. %: C, 66.73; H, 3.88; N, 14.97; Cl, 7.59. Found %: C, 66.60; H, 3.93; N, 14.86; Cl, 7.48.
 1H -NMR ($CDCl_3$): 2.10 (3H, s), 3.20 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m) (fig.119).

c: Brown crystals (54% yield), mp. 257 °C.

Analysis of $C_{25}H_{15}N_5O_3Cl$ (468.92). Calcd. %: C, 64.03; H, 3.22; N, 14.94; Cl, 7.57. Found %: C, 64.13; H, 3.16; N, 14.84; Cl, 7.66.
 1H -NMR ($CDCl_3$): 2.10 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m).

d: Brown crystals (60% yield), mp. > 340 °C.

Analysis of $C_{23}H_{14}N_5O_2Cl$ (427.89). Calcd. %: C, 64.56; H, 3.30; N, 16.37; Cl, 8.30. Found %: C, 64.43; H, 3.24; N, 16.25; Cl, 8.43.
 1H -NMR ($CDCl_3$): 2.10 (3H, s), 5.00 (1H, s), 6.20-8.35 (10H, m).

e: Brown crystals (63% yield), mp. 195 °C.

Analysis of $C_{23}H_{14}N_5OSCl$ (443.99). Calcd. %: C, 62.22; H, 3.18; N, 15.78; S, 7.23; Cl, 8.00. Found %: C, 62.36; H, 3.25; N, 15.67; S, 7.17; Cl, 8.11.
 1H -NMR ($CDCl_3$): 2.10 (3H, s), 5.00 (1H, s), 6.20-8.30 (10H, m).

7-Aryl-5-chloro-9-thioxo-7,10-dihydro[1,2,4]triazolo[3'',4'':3',4']-pyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines (248_{a-e}).

General procedure: A mixture of 246_{a-e} (0.01 mol) carbon disulfide (3 ml) in ethanol (30 ml) and two pellets of potassium hydroxide was heated under reflux on a water bath for 6h. The solid product obtained was dissolved in water then acidified with acetic acid and recrystallized from dioxane.

a: Brown crystals (59% yield), mp. 191 °C.

Analysis of $C_{24}H_{14}N_5OSCl$ (456). Calcd. %: C, 63.21; H, 3.10; N, 15.36; S, 7.04; Cl, 7.79. Found %: C, 63.32; H, 3.01; N, 15.45; S, 7.13; Cl, 7.88.
IR: 3222 (NH), 1190 (CS) (fig.12). MS, m/z: 456.02 (fig.120).
 1H -NMR (CF_3COOD): 5.10 (1H, s), 6.30-8.25 (12H, m).

b: Brown crystals (62% yield), mp. > 340 °C.

Analysis of $C_{25}H_{16}N_5O_2SCl$ (486.03). Calcd. %: C, 61.78; H, 3.32; N, 14.41; S, 6.61; Cl, 7.30. Found %: C, 61.89; H, 3.38; N, 14.32; S, 6.62; Cl, 7.41.

$^1\text{H-NMR}$ (CF_3COOD): 3.50 (3H, s), 5.10 (1H, s), 6.30-8.30 (11H, m).

c: Brown crystals (58% yield), mp. 263 °C.

Analysis of $\text{C}_{24}\text{H}_{13}\text{N}_6\text{O}_3\text{SCl}$ (501). Calcd. %: C, 57.53; H, 2.62; N, 16.78;

S, 6.41; Cl, 7.09. Found %: C, 7.43; H, 2.56; N, 16.86; S, 6.50; Cl, 7.19.

IR: 3350 (NH), 1190 (CS).

d: Brown crystals (65% yield), mp. 127 °C.

Analysis of $\text{C}_{22}\text{H}_{12}\text{N}_5\text{O}_2\text{SCl}$ (445.97). Calcd. %: C, 59.25; H, 2.71; N, 15.71;

S, 7.20; Cl, 7.96. Found %: C, 59.37; H, 2.65; N, 15.62; S, 7.12; Cl, 7.84.

IR: 3325 (NH), 1195 (CS).

$^1\text{H-NMR}$ (CDCl_3): 5.10 (1H, s), 6.20-8.30 (10H, m).

e: Brown crystals (67% yield), mp. > 340 °C.

Analysis of $\text{C}_{22}\text{H}_{12}\text{N}_5\text{OS}_2\text{Cl}$ (462.07). Calcd. %: C, 57.18; H, 2.62; N, 15.16;

S, 13.89; Cl, 7.68. Found %: C, 57.29; H, 2.56; N, 15.24; S, 13.78; Cl, 7.57.

IR: 3340 (NH), 1180 (CS).

$^1\text{H-NMR}$ (CF_3COOD): 5.10 (1H, s), 6.20-8.30 (10H, m).

List of Compounds

List of new compounds

Compd. No.

1- 2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines	218 _{a-e}
2- Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate	219 _{a-e}
3- 7-Aryl-5-chloro-10-methyl-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]-pyrano[3,2-h]quinolines	220 _{a-e}
4- 8-Amino-7-aryl-5-chloro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]quinolines	221 _{a-e}
5- 7-Aryl-5-chloro-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]-quinolines	222 _{a-e}
6- 4-Aryl-6-chloro-3-cyano-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]-quinolines	223 _{a-e}
7- 7-Aryl-5-chloro-8-imino-9-phenyl-7H-pyrimido[4',5':6,5]pyrano[3,2-h]-quinolines	224 _{a-e}
8- 8-Amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano[3,2-h]-quinolines	225 _{a-e}
9- 5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines	226 _{a-e}
10- 2-Amino-4-aryl-3-(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]-quinolines	227 _{a-c}
11- 2,3,14-Trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines	228 _{a-e}
12- 2,3,5,6,14-Pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines	229 _{a-e} – 232 _{a-c}
13- 5-Thioxo-2,3,6,14-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2h]quinolines	233 _{a-e}
14- 5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines	234 _{a-c}
15- 14-Aryl-12-chloro[1,2,4]triazolo[3'',4''-f][1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines	235 _{a-c}
16- 14-Aryl-12-chloro-3-thioxo[1,2,4]triazolo[3'',4''-f][1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines	236 _{a-c}
17- 5-Aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines	237 _{a-e}
18- Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylates	238 _{a-e}
19- 2-(1-pyrrolyl)-4aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbohydrazide	239 _{a-e}
20- 2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines	240 _{a-e}
21- 2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-oylazid	241 _{a-e}
22- Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbamate	242 _{a-c}
23- 4-[2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-yl]-semicarbazide	243 _{a-e}
24- 7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines	244 _{a-e}
25- 7-Aryl-5,9-dichloropyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines	245 _{a-e}
26- 7-Aryl-5-chloro-9-hydrazinopyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines	246 _{a-c}

- 27- 7-Aryl-5-chloro-9-methyl[1,2,4]triazolo[3",4":3',4']pyrrolo[1",2":1',2']-
pyrazino[5',6':5,6] pyrano[3,2-h]quinolines 247_{a-c}
- 28- 7-Aryl-5-chloro-9-thioxo-7,10-dihydro[1,2,4]triazolo[3",4":3',4']-
pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines 248_{a-c}

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Appendix

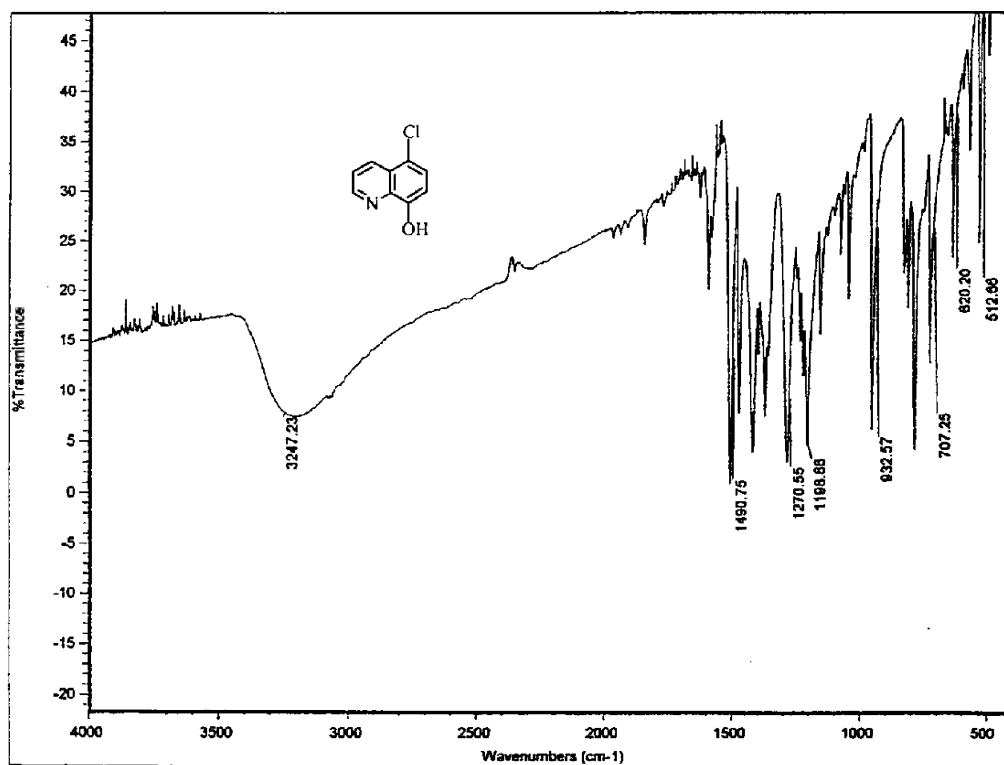
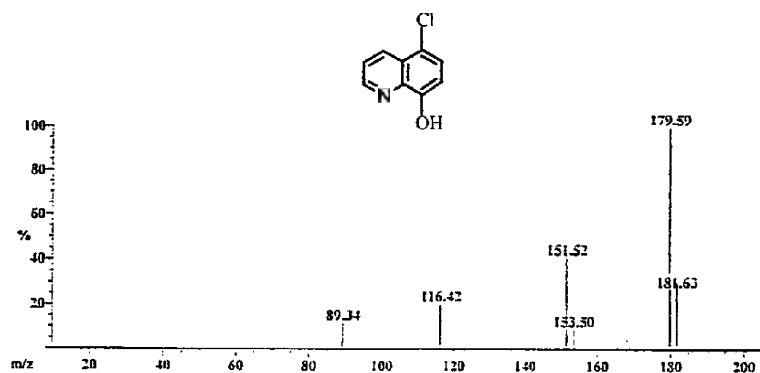


Fig.(1): 5-Chloro-8-quinolinol (217).

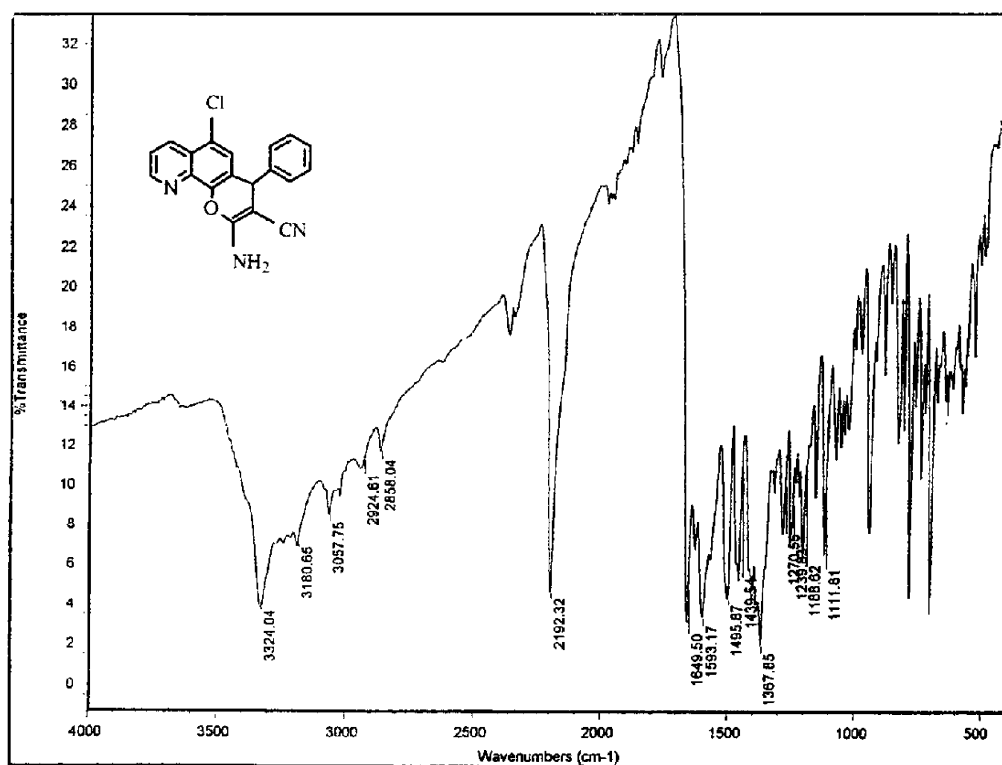


Fig.(2): 2-Amino-6-chloro-3-cyano-4-phenyl-4H-pyrano[3,2-h]quinoline (**218_a**).

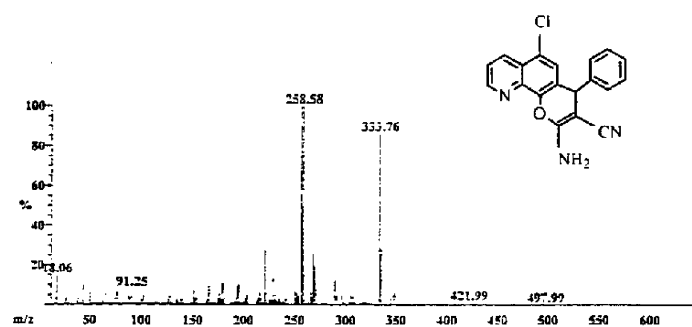
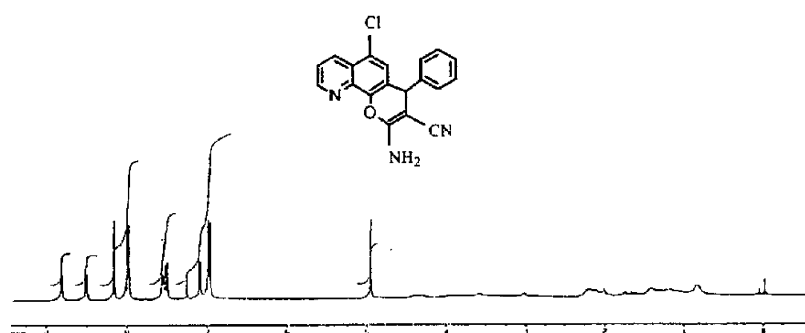


Fig.(3): 2-Amino-6-chloro-3-cyano-4-phenyl-4H-pyrano[3,2-h]quinoline (**218_a**).

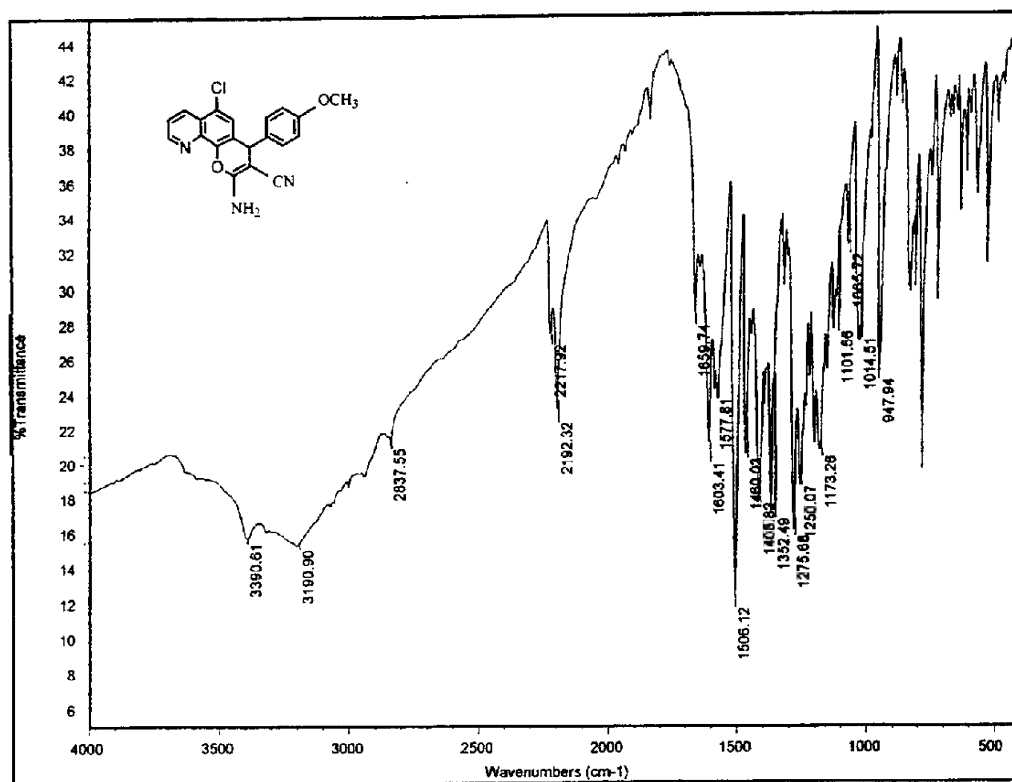


Fig.(4): 2-Amino-6-chloro-3-cyano-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline (**218_b**).

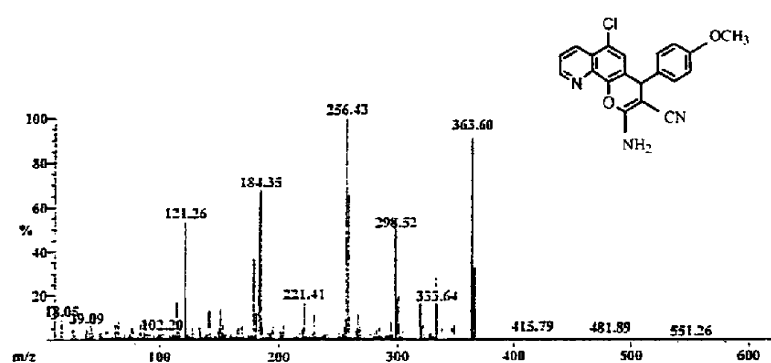


Fig.(5): 2-Amino-6-chloro-3-cyano-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline (**218_b**).

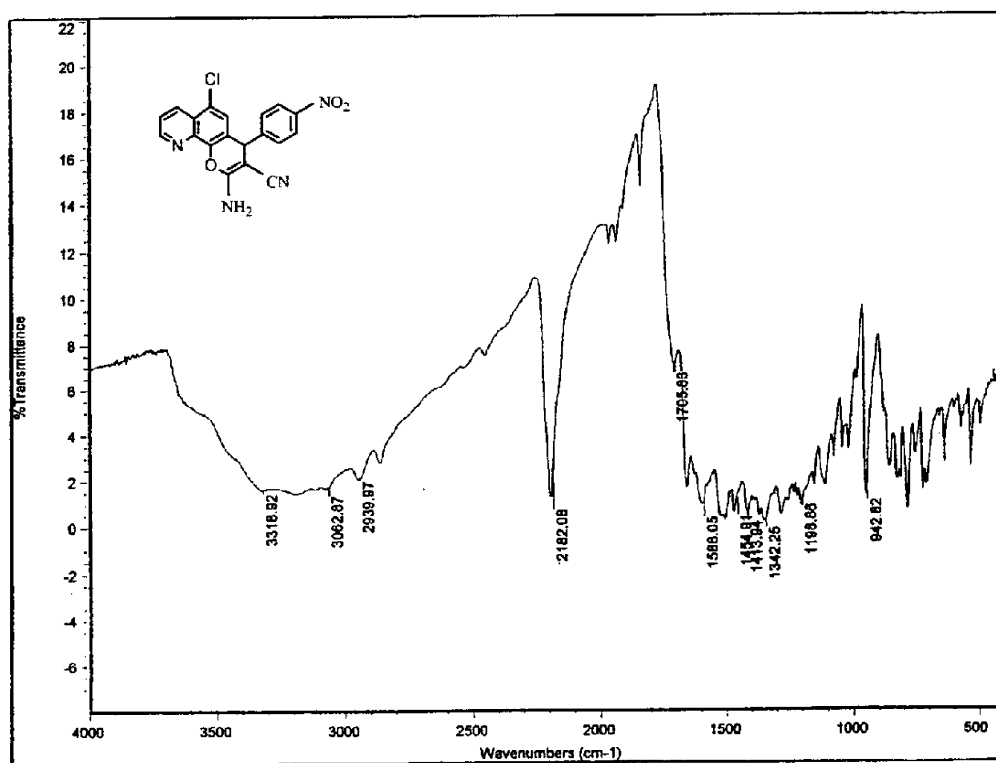


Fig.(6): 2-Amino-6-chloro-3-cyano-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline (**218c**).

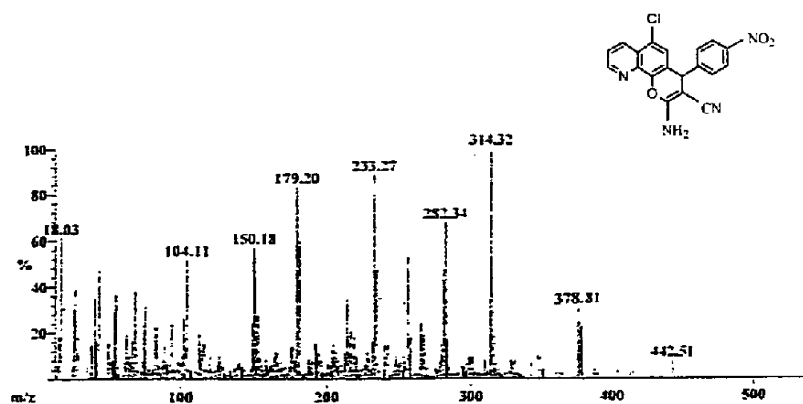
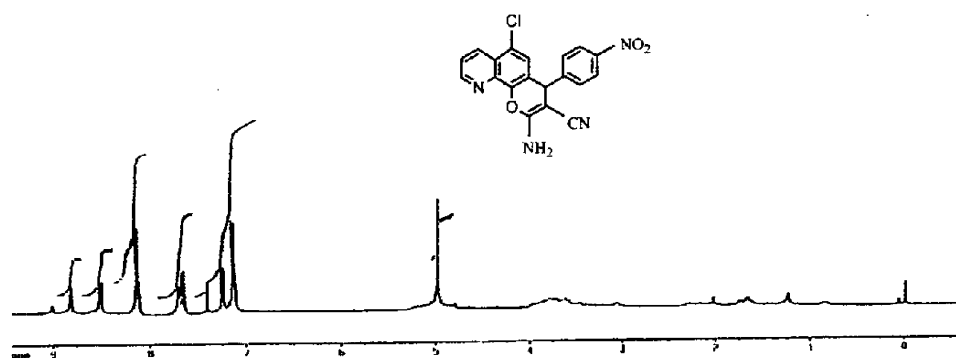


Fig.(7): 2-Amino-6-chloro-3-cyano-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline (218_c).

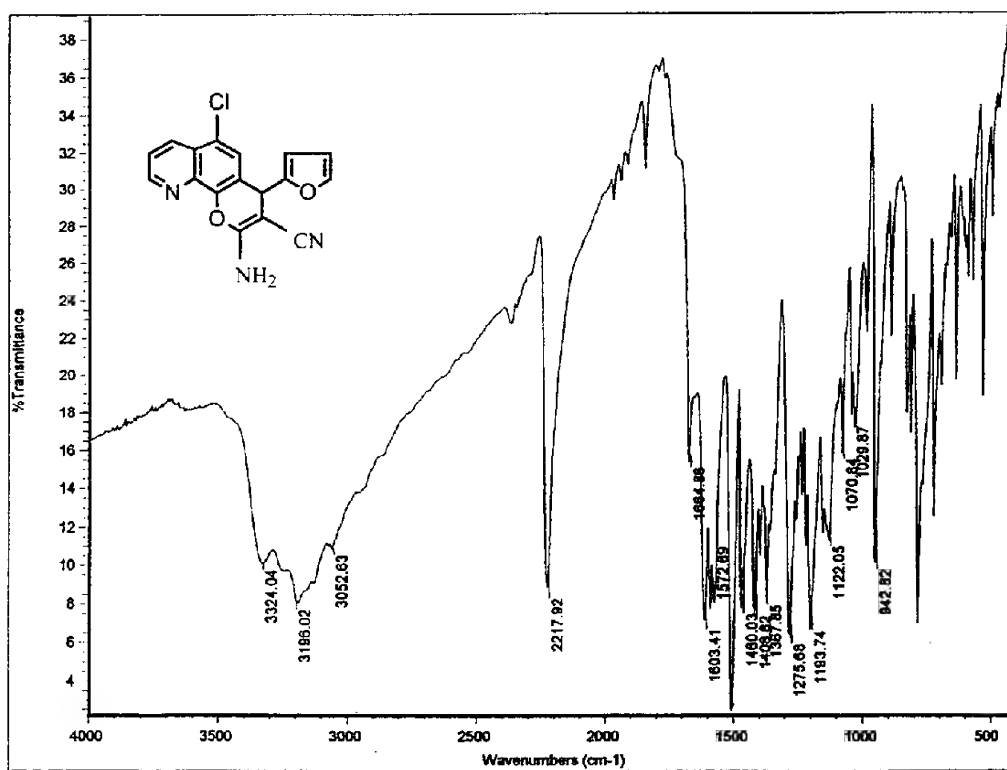
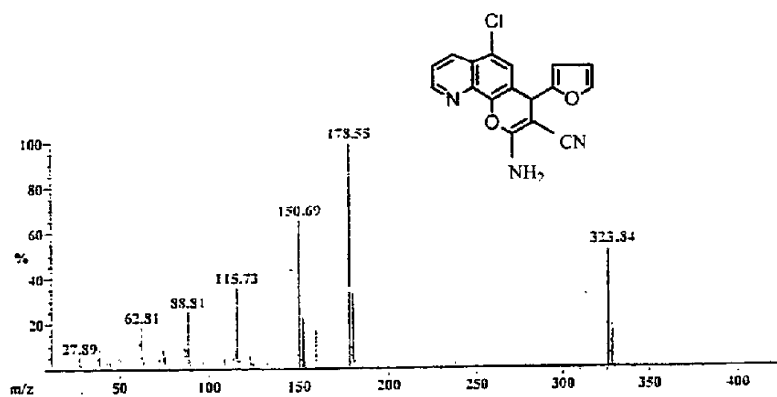


Fig.(8): 2-Amino-6-chloro-3-cyano-4-furyl-4H-pyrano[3,2-h]quinoline (218_d).

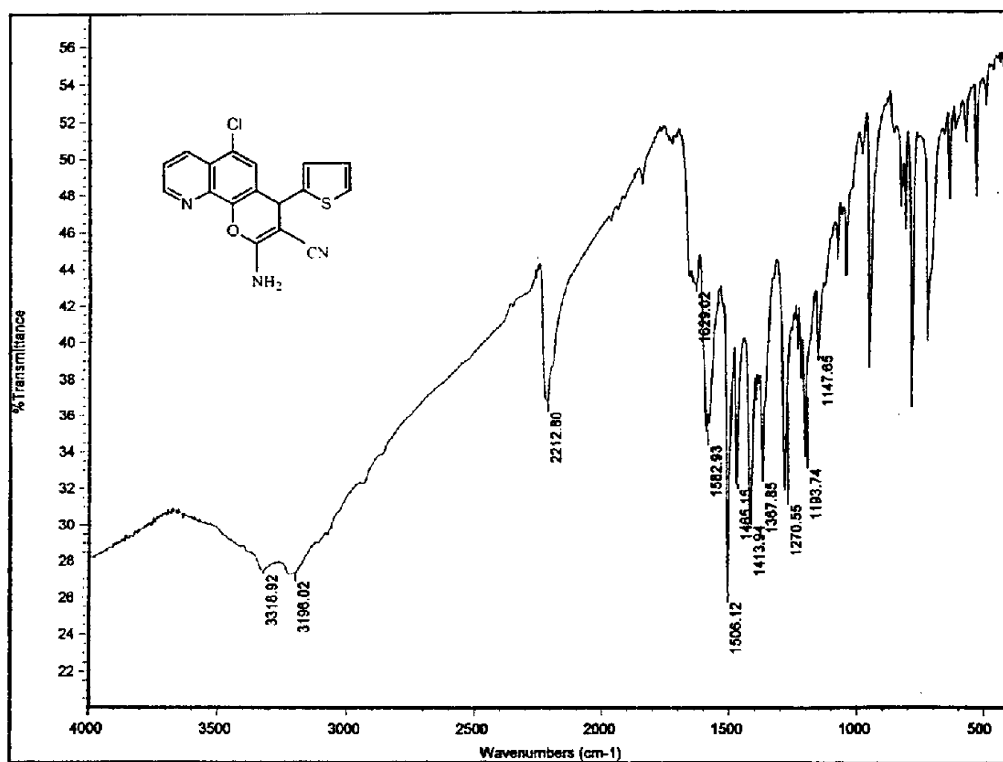
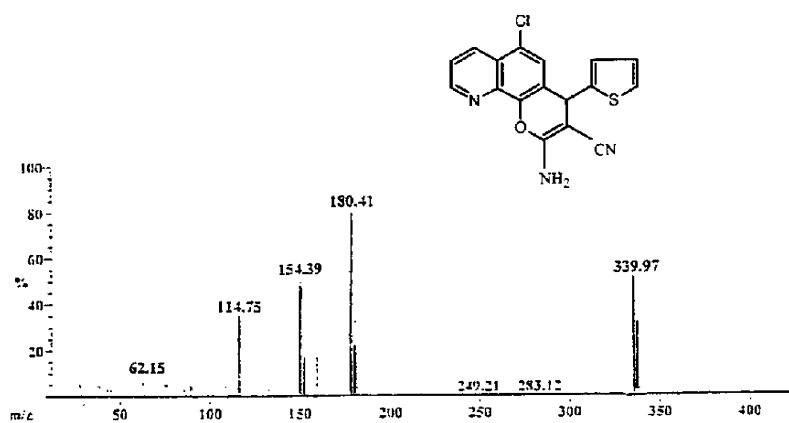


Fig.(9): 2-Amino-6-chloro-3-cyano-4-thienyl-4H-pyrano[3,2-h]quinoline (**218_c**).

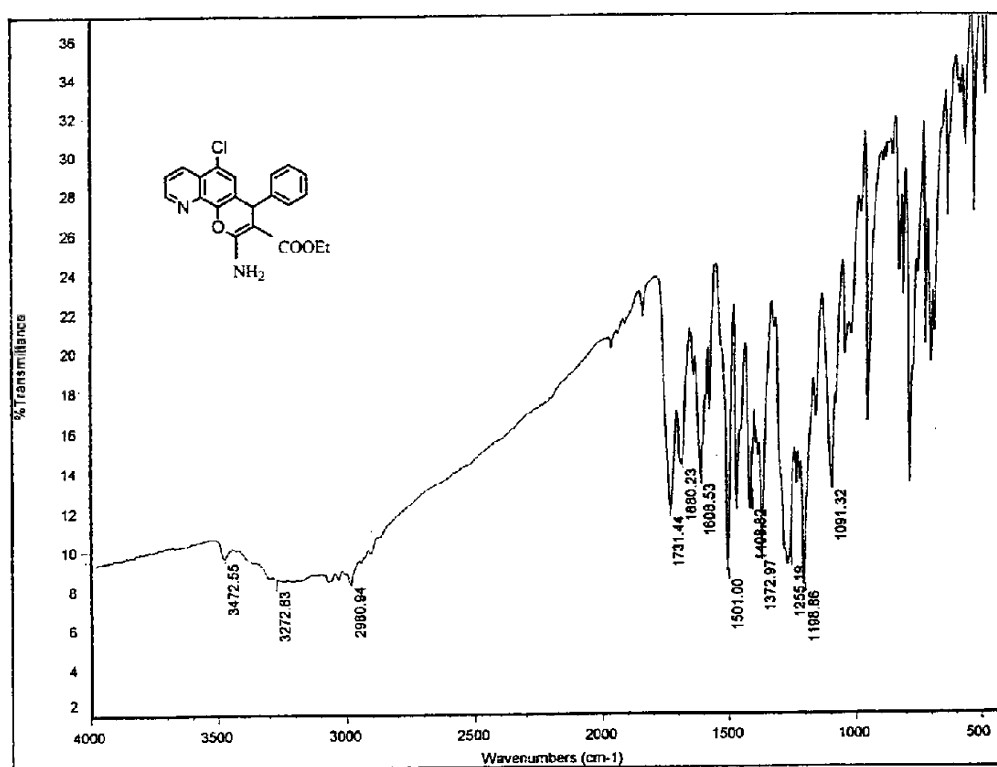


Fig.(10): Ethyl 2-amino-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219_a**).

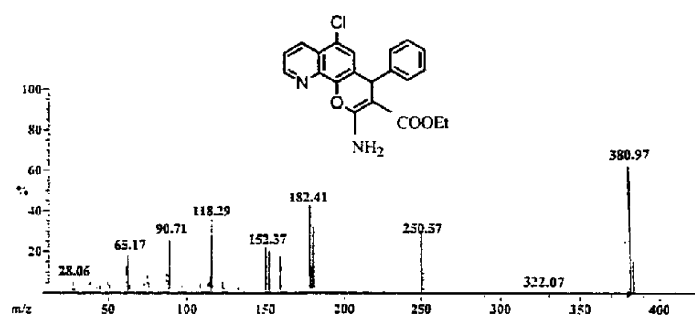


Fig.(11): Ethyl 2-amino-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219_a**).

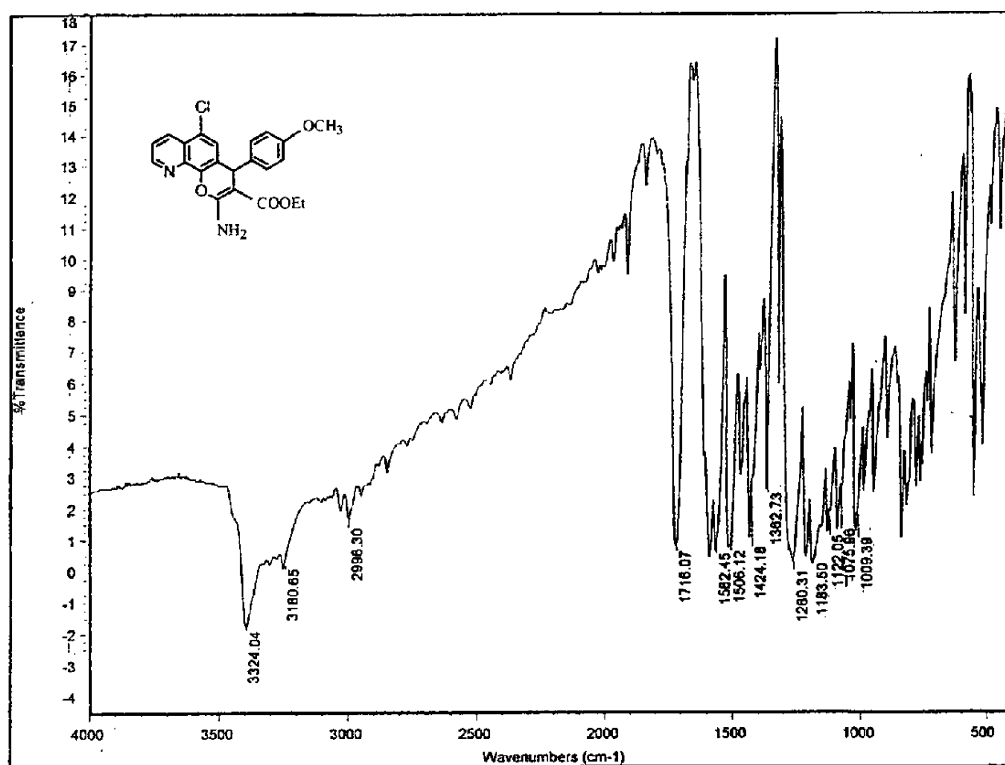


Fig.(12): Ethyl 2-amino-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate (**219_b**).

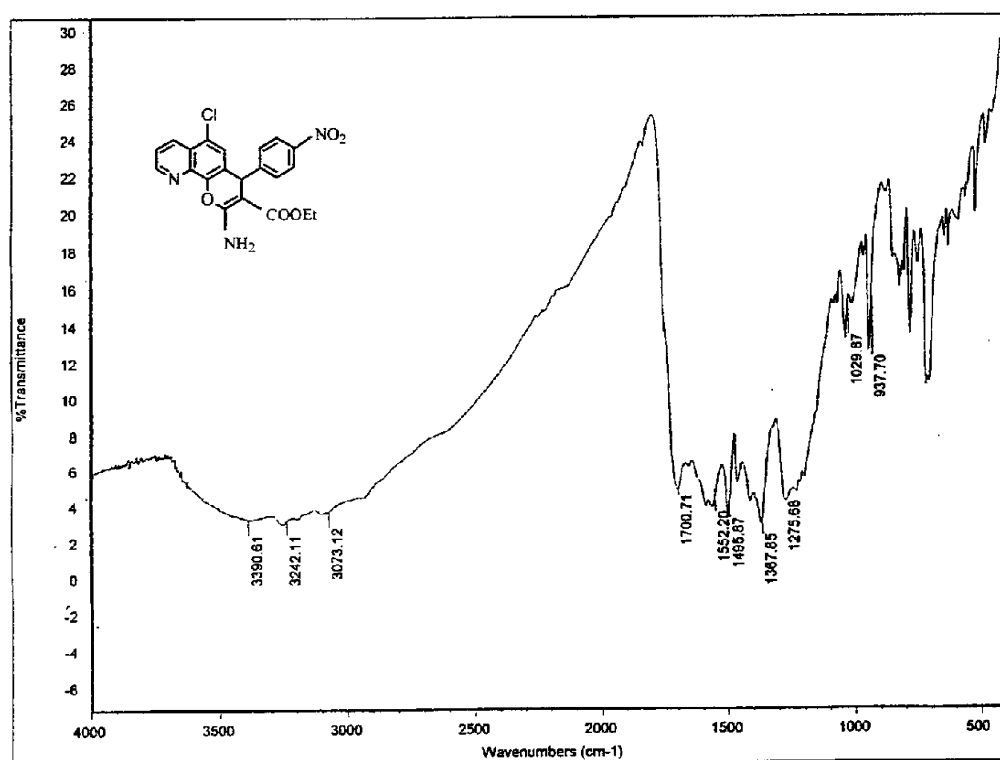


Fig.(13): Ethyl 2-amino-6-chloro-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate (**219c**).

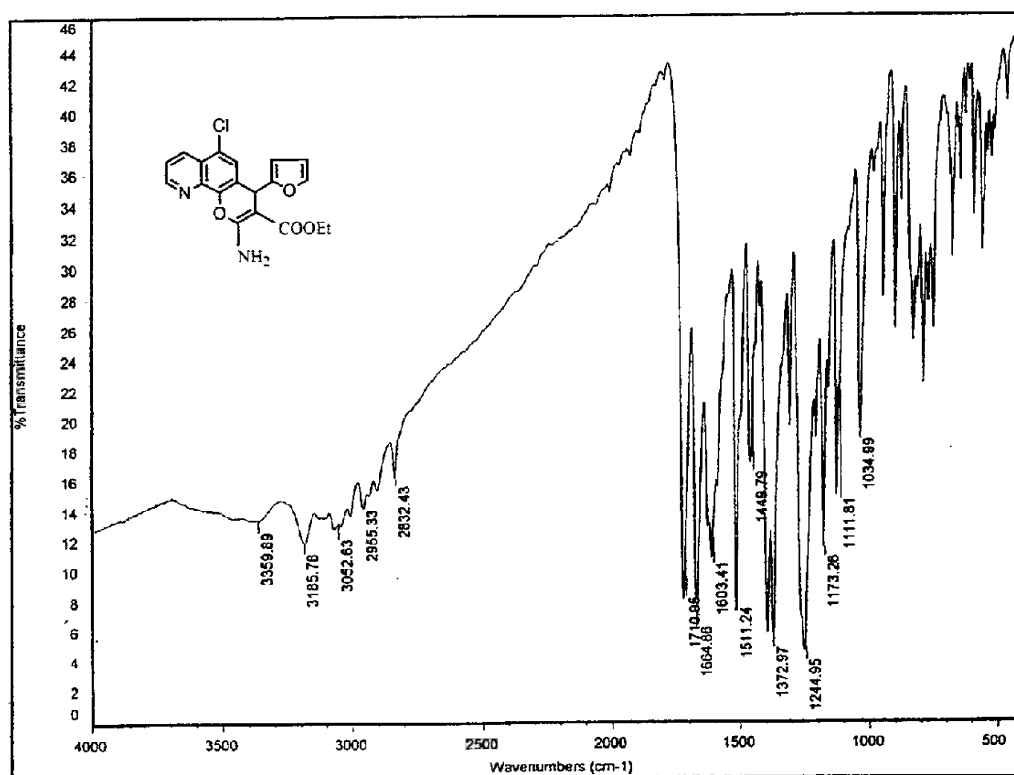


Fig.(14): Ethyl 2-amino-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219_d**).

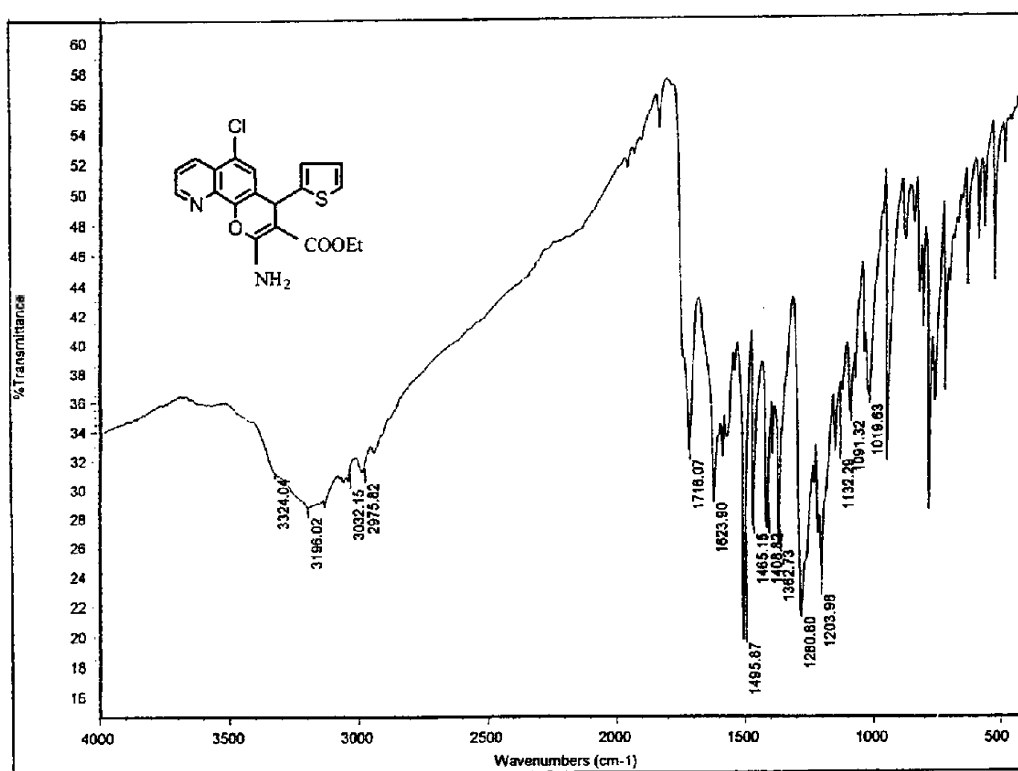


Fig.(15): Ethyl 2-amino-6-chloro-4-thienyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219e**).

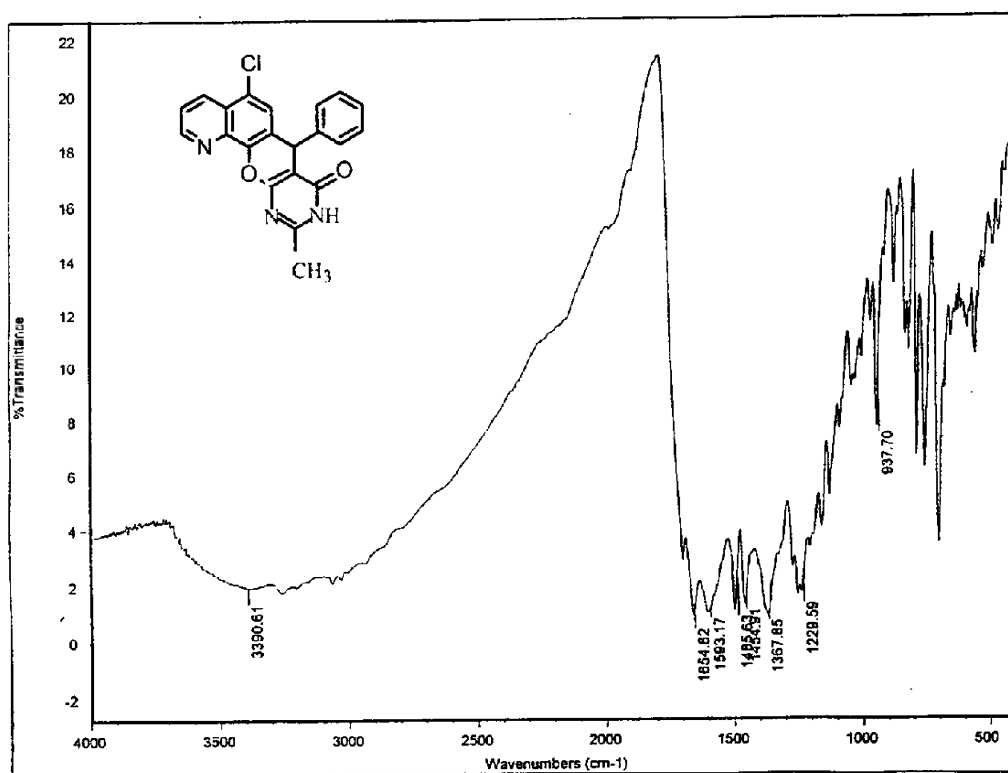
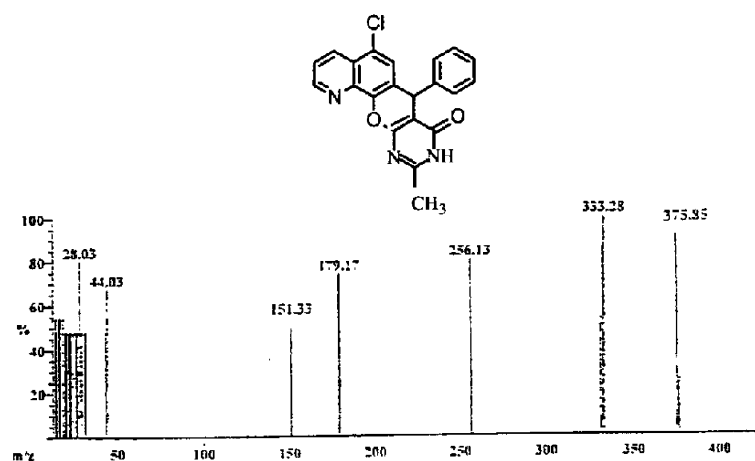


Fig.(16): 5-Chloro-10-methyl-7-phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]-pyrano[3,2-h]quinoline (**220_a**).

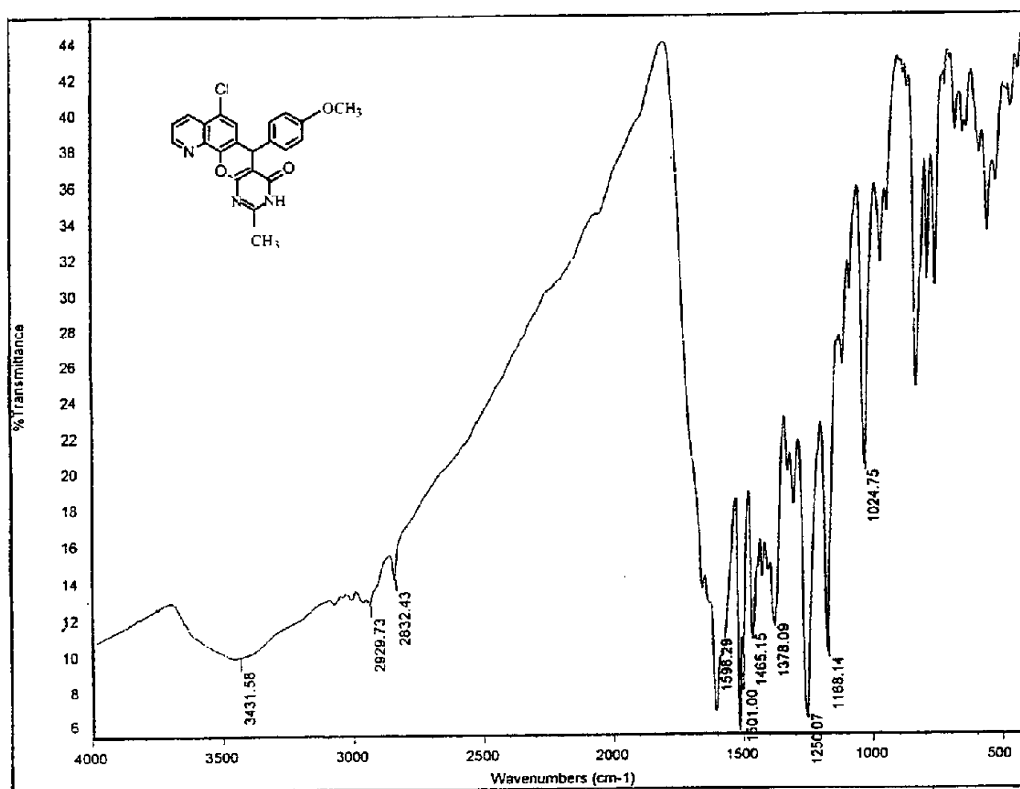
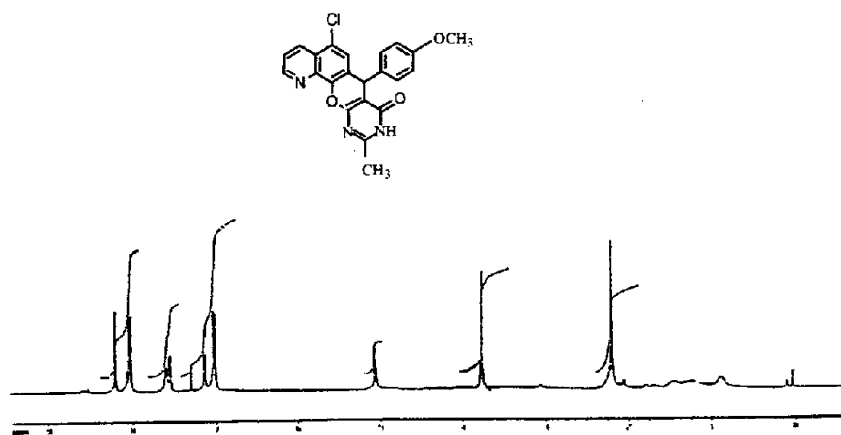


Fig.(17): 5-Chloro-10-methyl-7-(4-methoxy)phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]pyrano[3,2-h]quinoline (220_b).

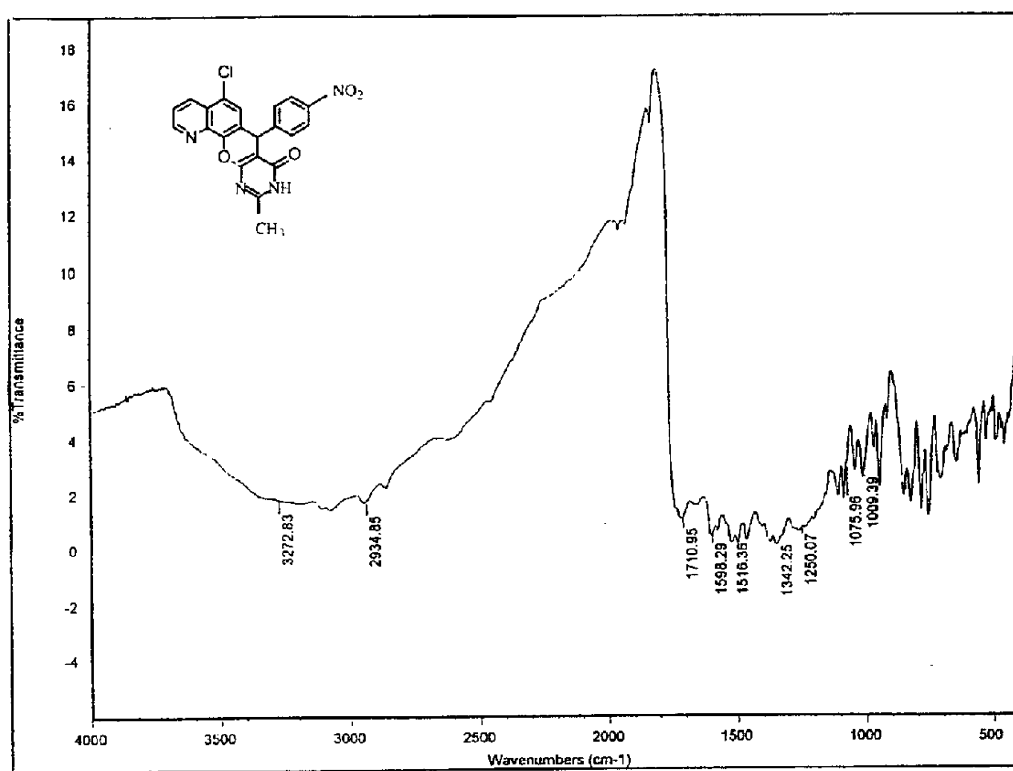
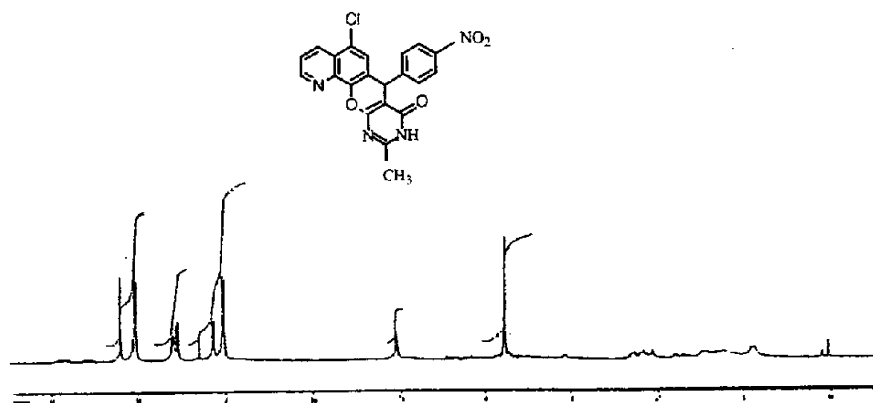


Fig.(18): 5-Chloro-10-methyl-7-(4-nitro)phenyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline (**220_c**).

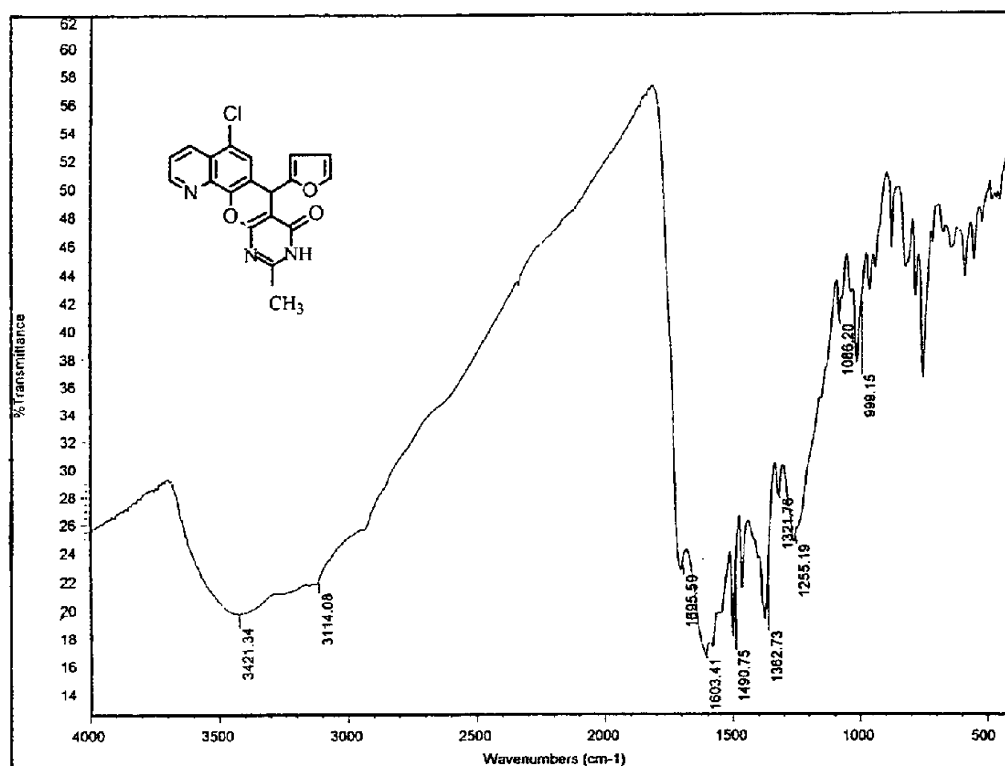


Fig.(19): 5-Chloro-10-methyl-7-furyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline (**220d**).

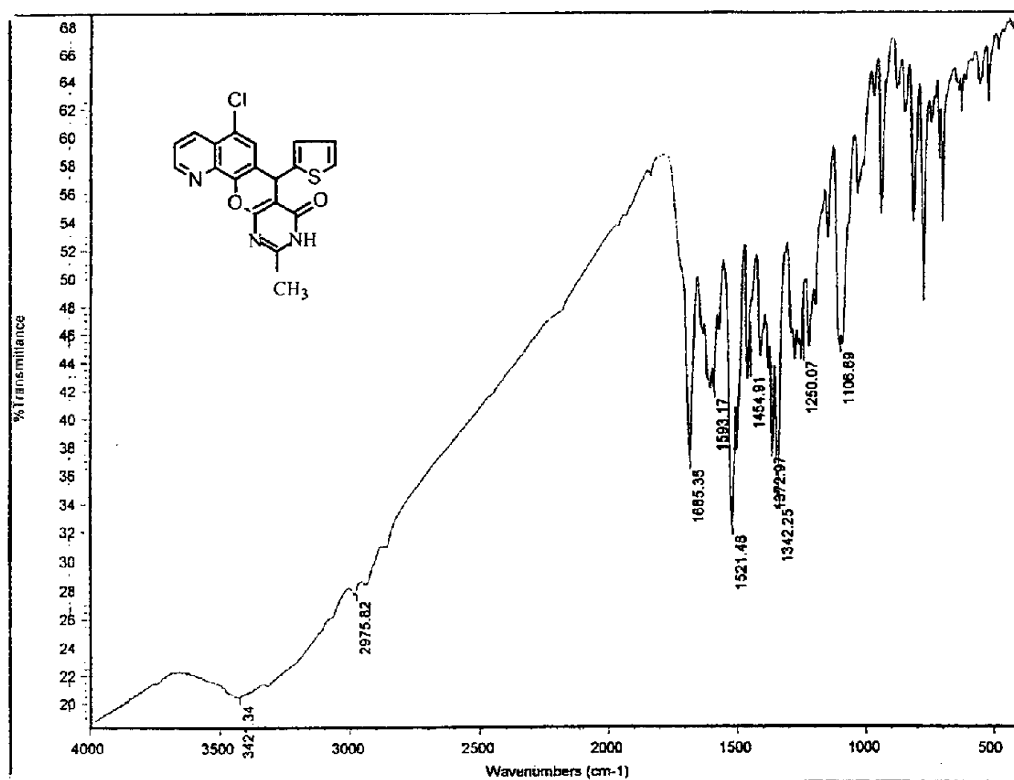


Fig.(20): 5-Chloro-10-methyl-7-thienyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline (**220_c**).

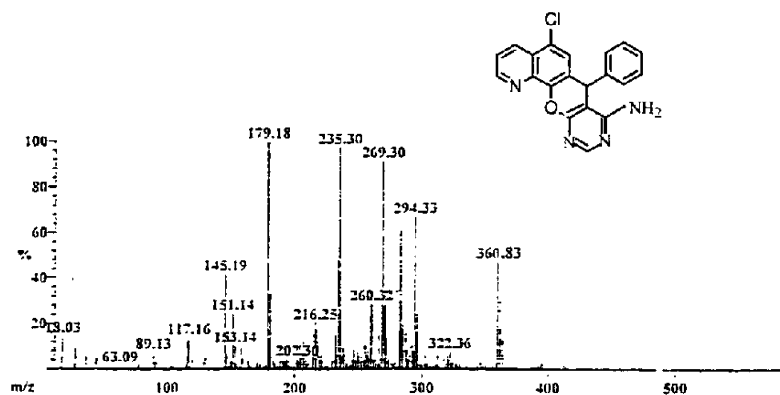
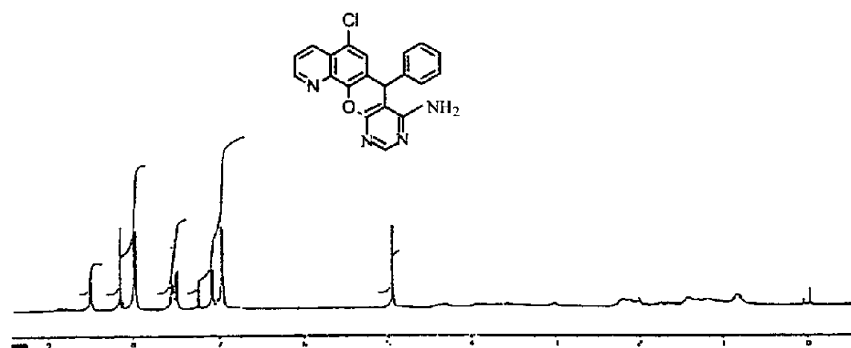


Fig.(21): 8-Amino-5-chloro-7-phenyl-7H-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (221_a).

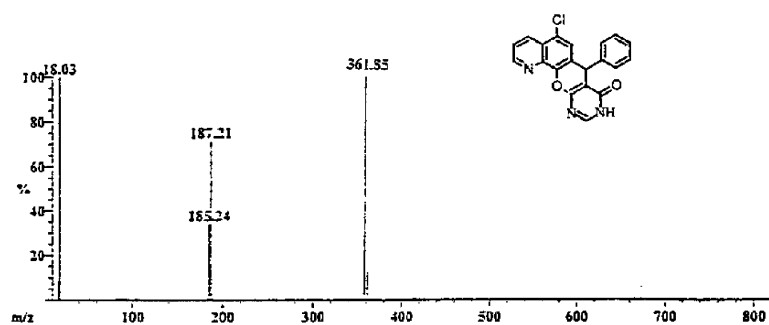


Fig.(22): 5-Chloro-7-phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**222_a**).

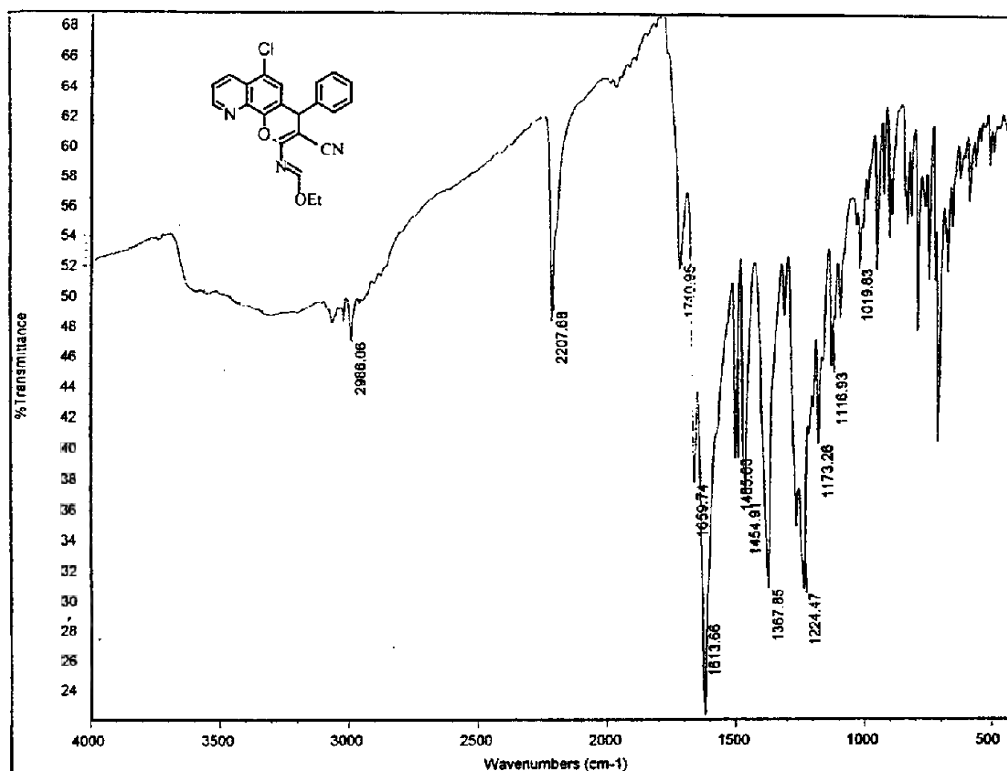


Fig.(23): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-phenyl-4H-pyrano-[3,2-h]quinoline (**223_a**).

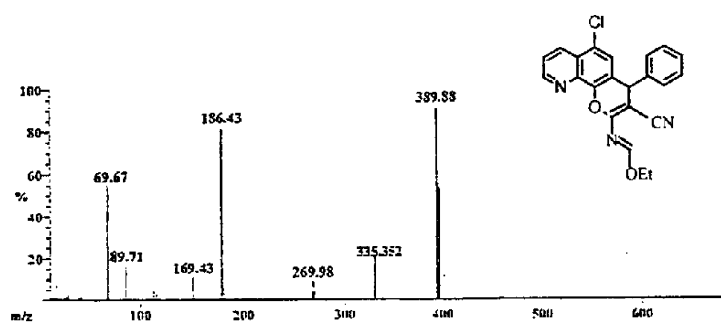


Fig.(24): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-phenyl-4H-pyrano-[3,2-b]quinoline (**223_a**).

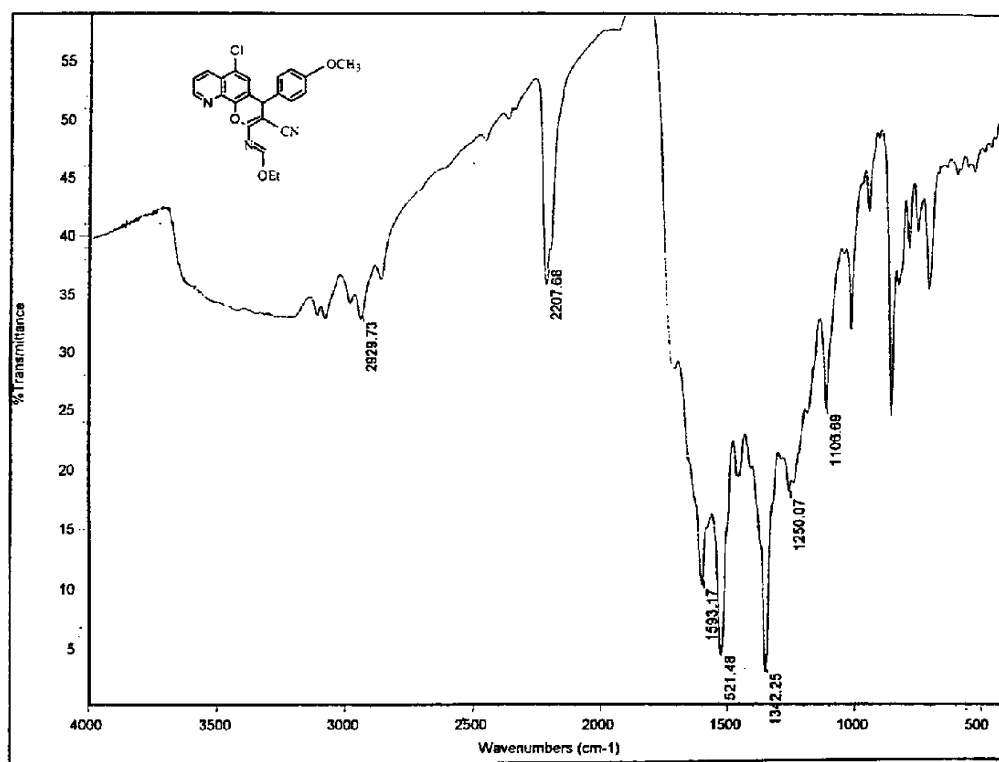


Fig.(25): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-(4-methoxy)phenyl-4H-pyrano[3,2-h]quinoline (**223_b**).

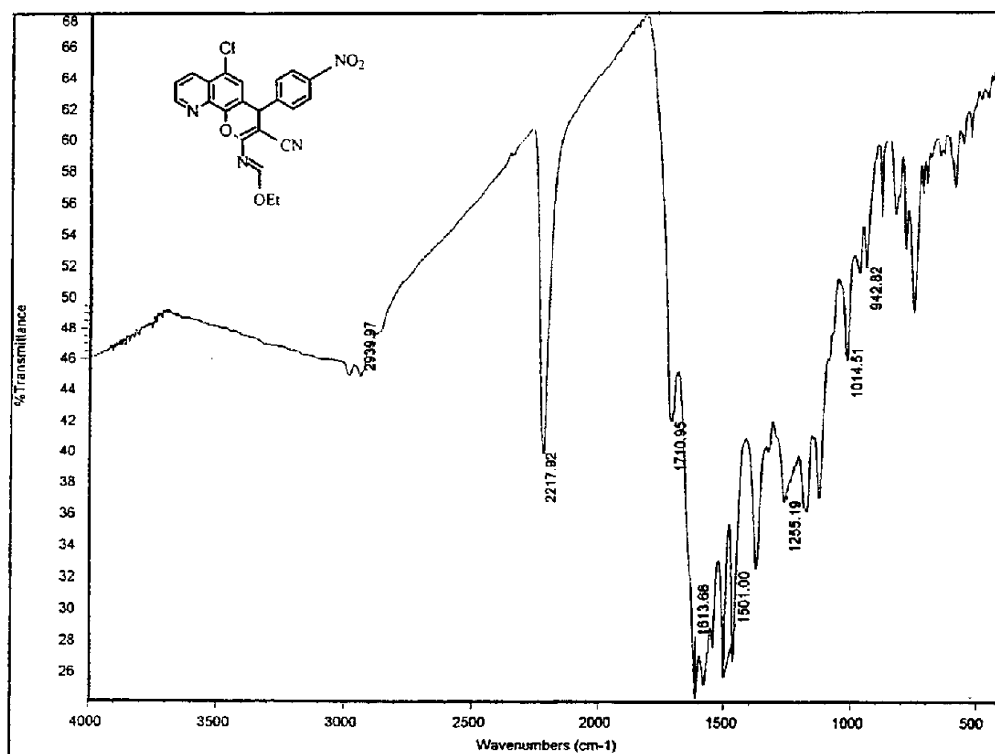


Fig.(26): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-(4-nitro)phenyl-4H-pyrano[3,2-h]quinoline (**223c**).

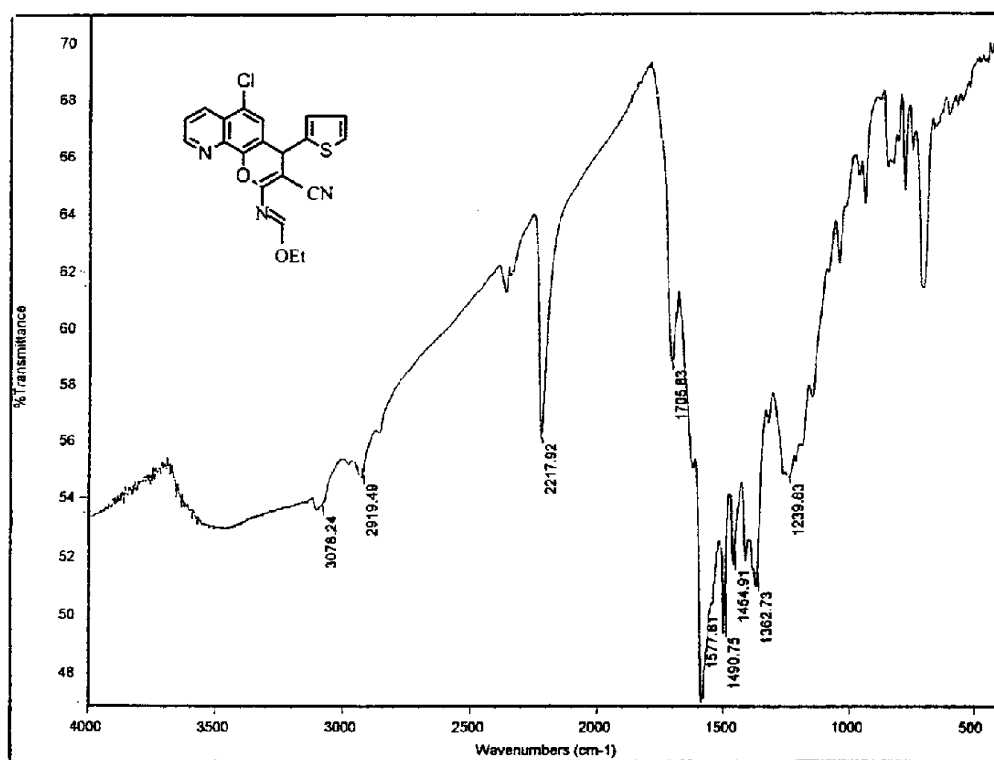


Fig.(27): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-thienyl-4H-pyrano-[3,2-b]quinoline (**223c**).

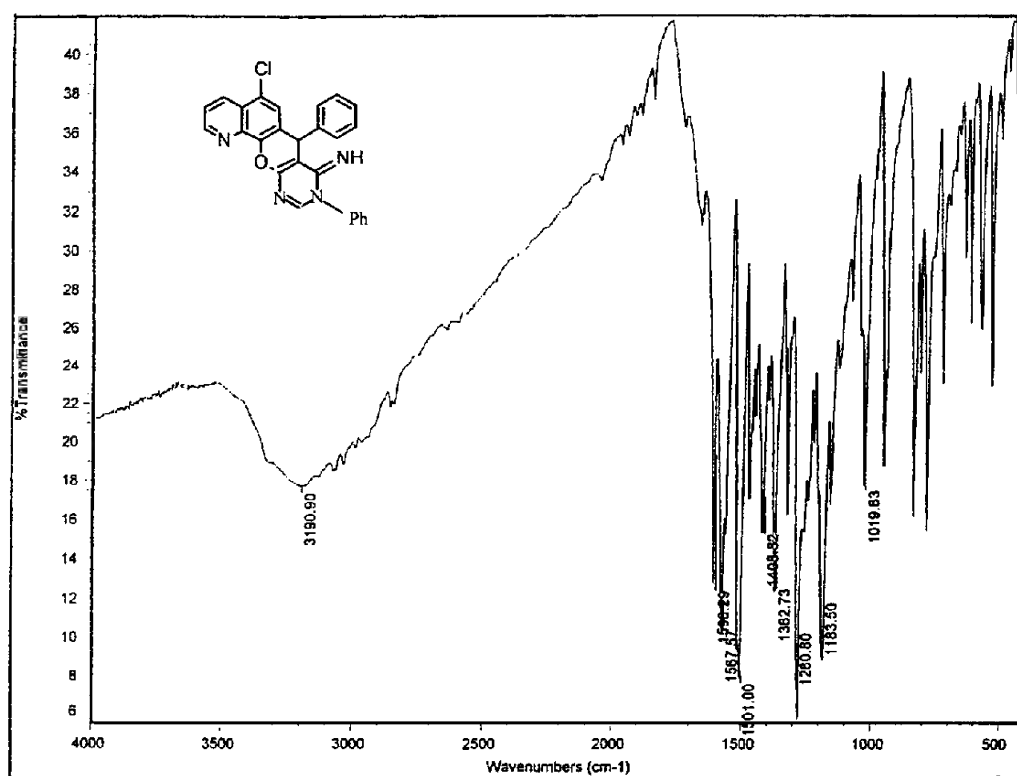


Fig.(28): 5-Chloro-7,9-diphenyl-8-imino-7H-pyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**224_a**).

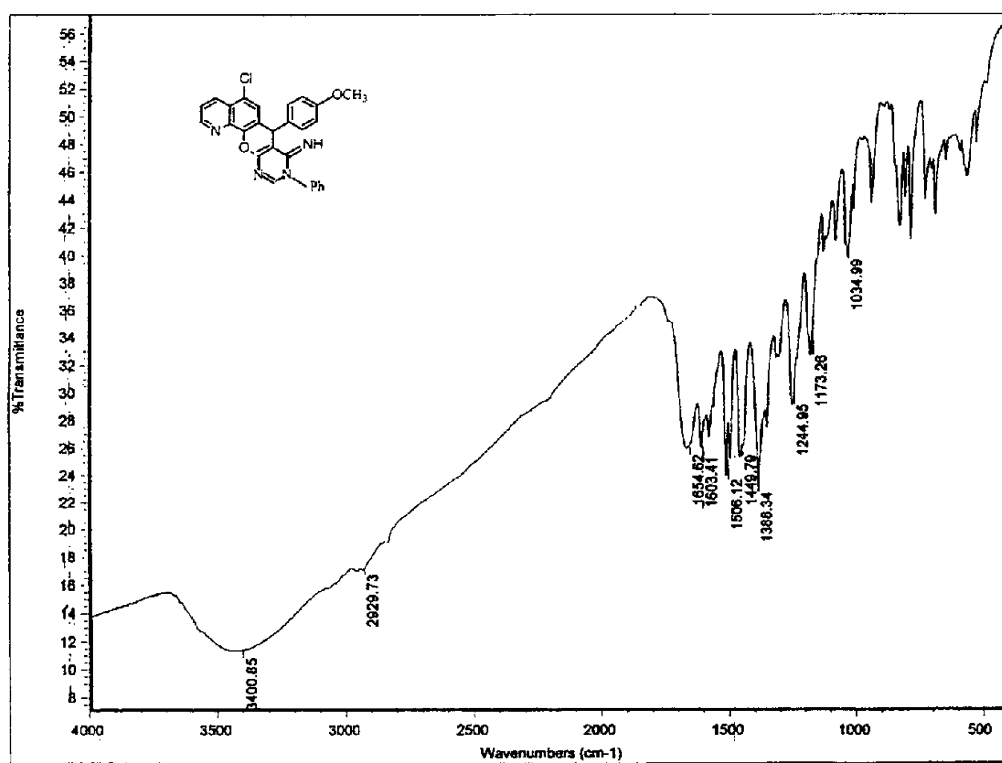
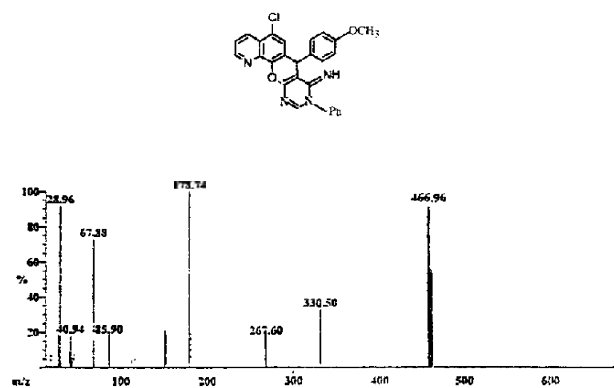


Fig.(29): 5-Chloro-8-imino-7-(4-methoxy)phenyl-7H-9-phenylpyrimido-[4',5':6,5]pyrano[3,2-h]quinoline (**224_b**).

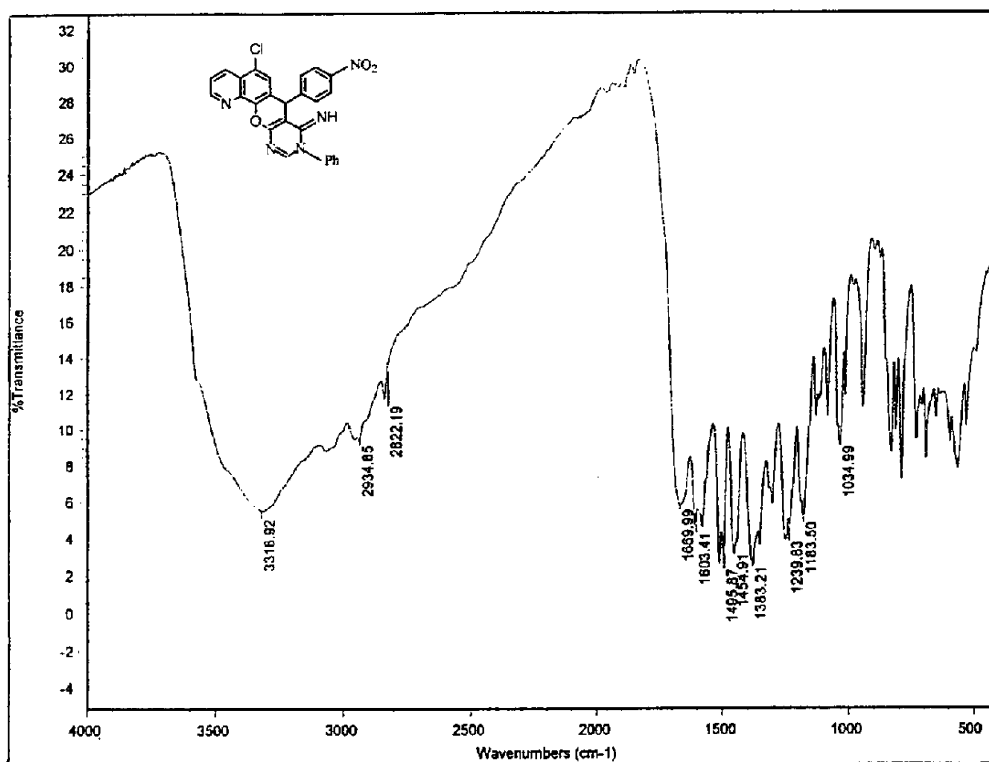


Fig.(30): 5-Chloro-8-imino-7-(4-nitro)phenyl-7H-9-phenylpyrimido-[4',5':6,5]pyrano[3,2-h]quinoline (**224c**).

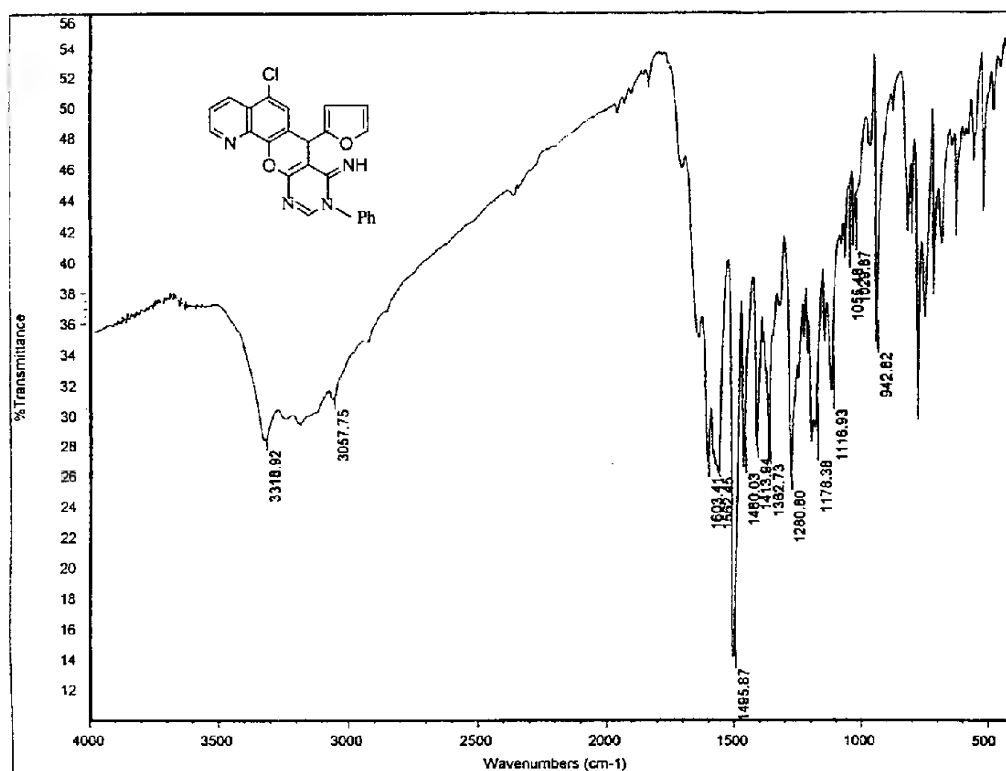


Fig.(31): 5-Chloro-8-imino-7-furyl-7H-9-phenylpyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**224_d**).

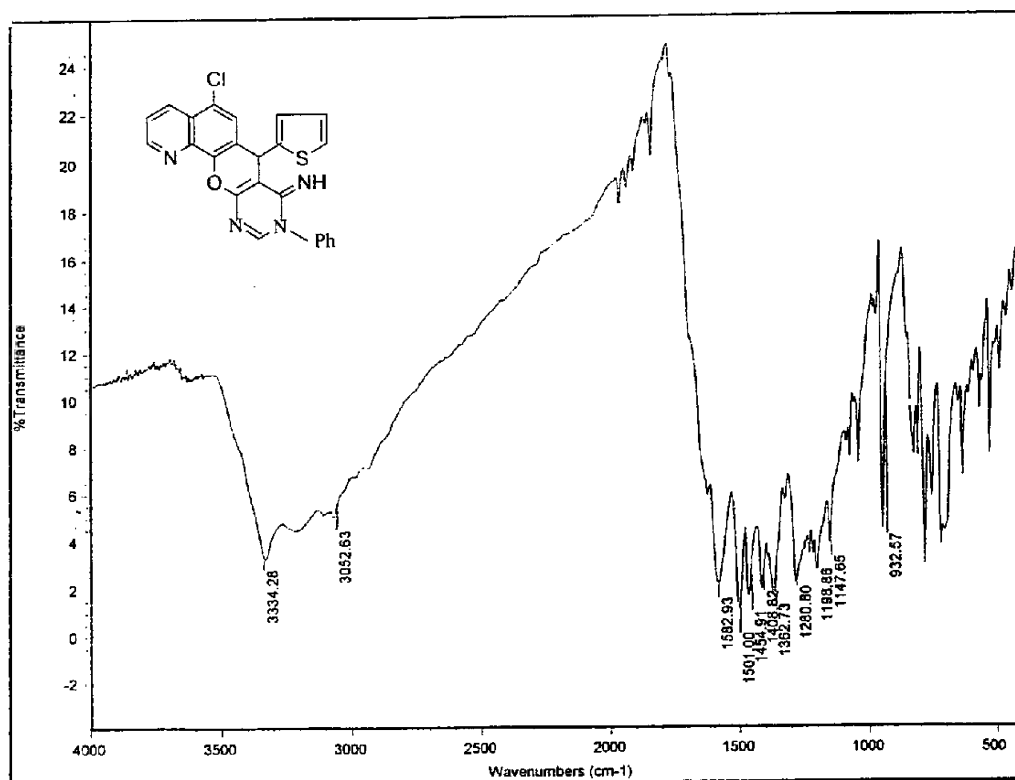


Fig.(32): 5-Chloro-8-imino-7-thienyl-7H-9-phenylpyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**224_c**).

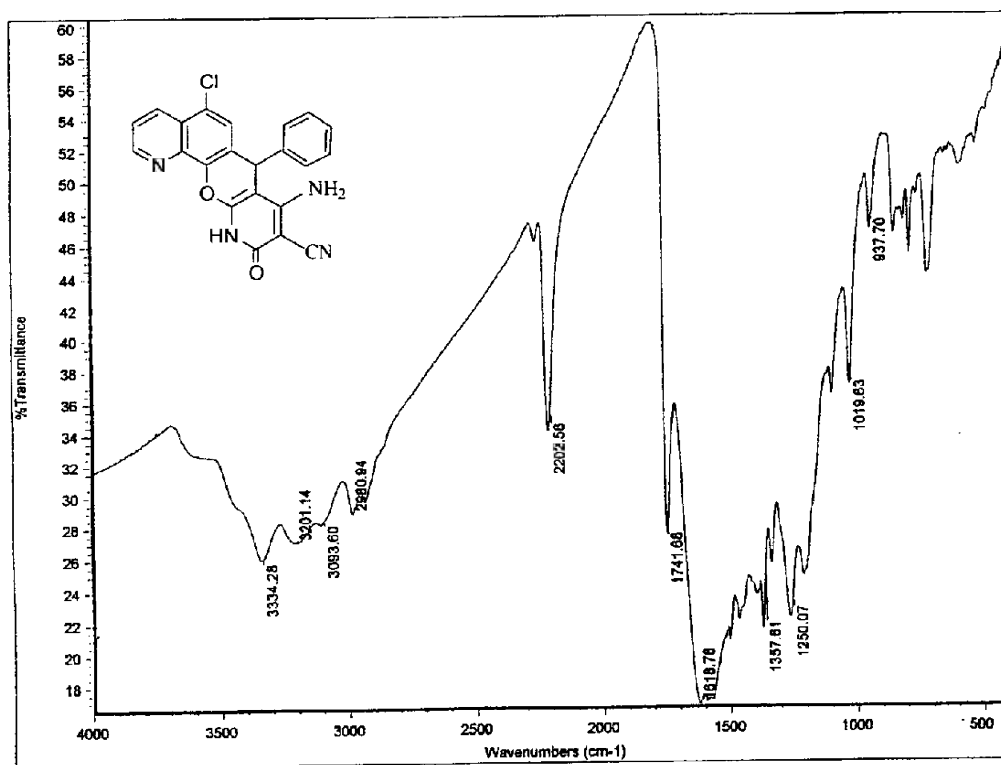


Fig.(33): 8-Amino-5-chloro-9-cyano-7-phenyl-7H-10-oxo-10,11-dihydropyrido-[2',3':6,5]pyrano[3,2-h]quinoline (**225_a**).

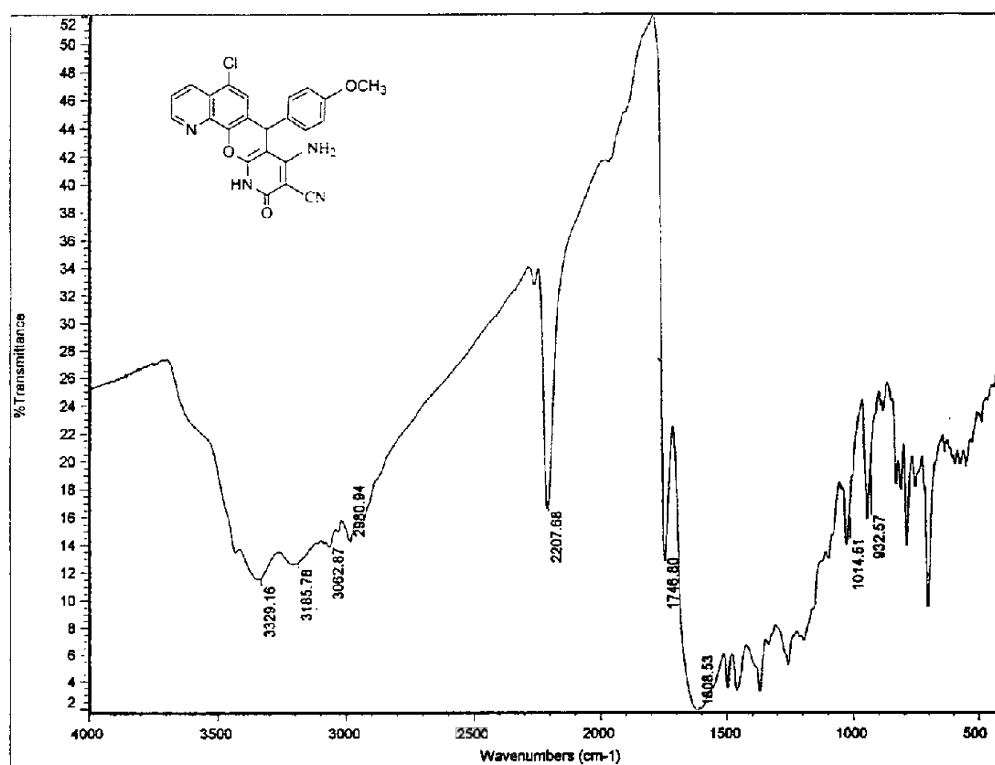
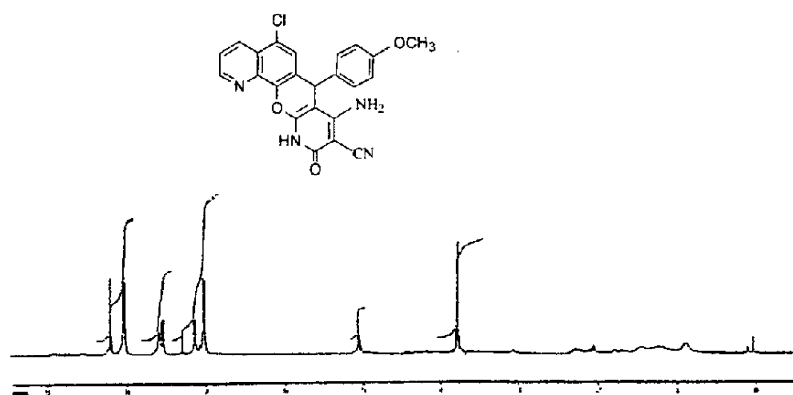


Fig.(34): 8-Amino-5-chloro-9-cyano-7-(4-methoxy)phenyl-7H-10-oxo-10,11-dihydropyrido[2',3':6,5]pyrano[3,2-h]quinoline (**225_b**).

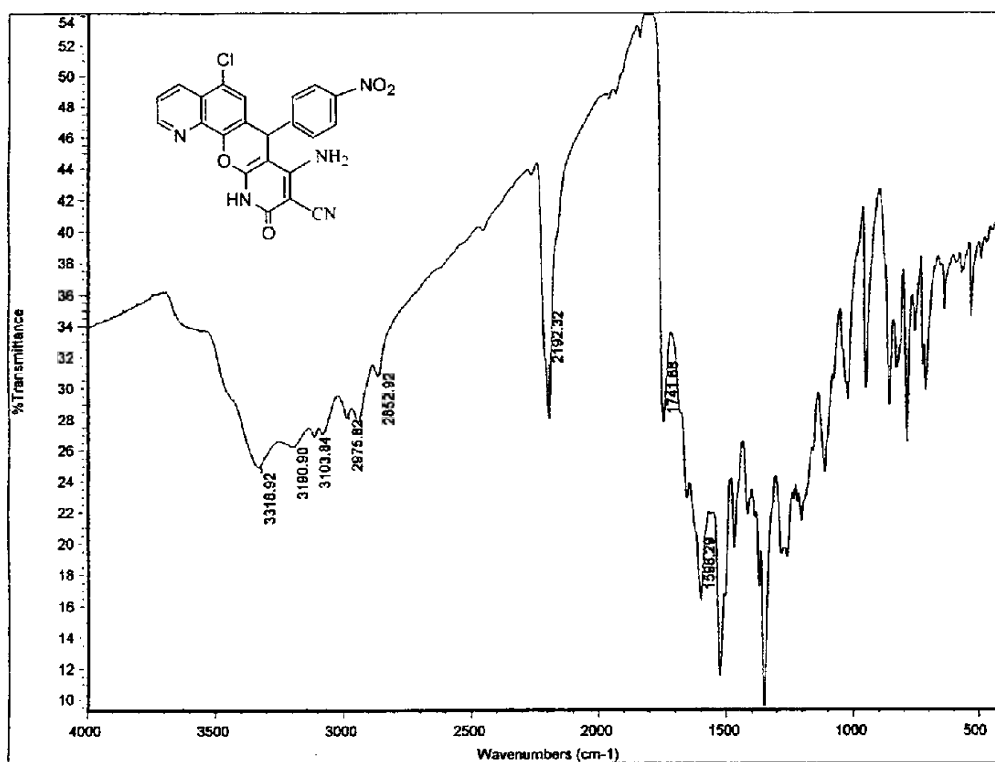


Fig.(35): 8-Amino-5-chloro-9-cyano-7-(4-nitro)phenyl-7H-10-oxo-10,11-dihydropyrido[2',3':6,5]pyrano[3,2-h]quinoline (**225c**).

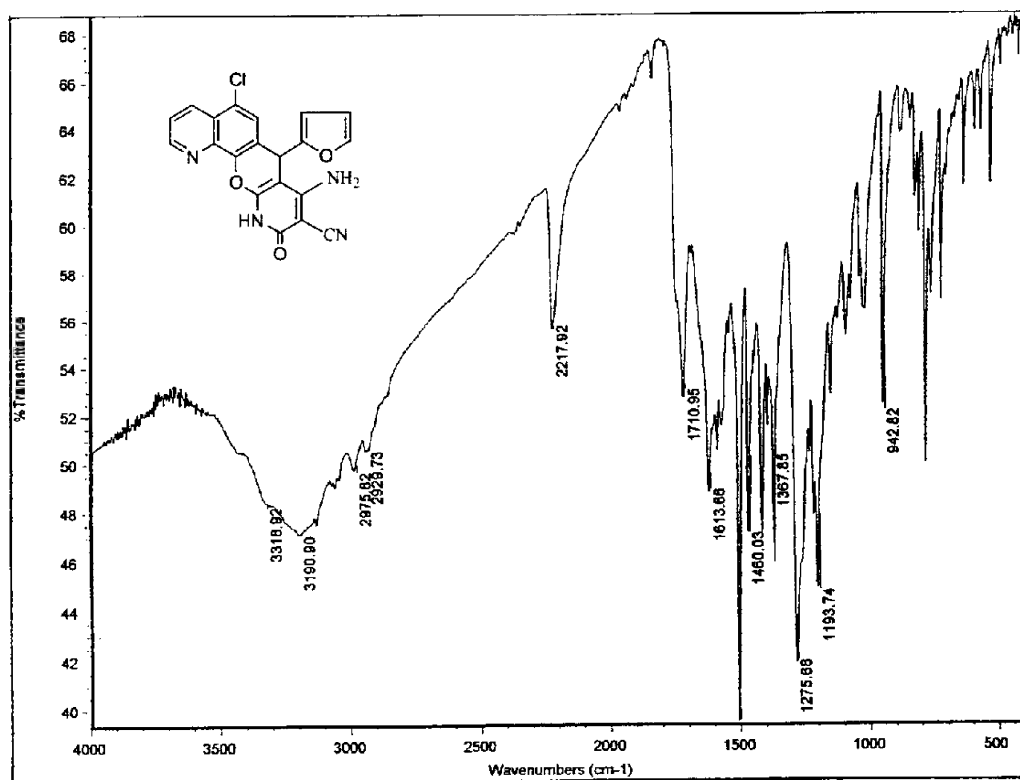


Fig.(36): 8-Amino-5-chloro-9-cyano-7-furyl-7H-10-oxo-10,11-dihydropyrido [2',3':6,5]pyrano[3,2-h]quinoline (**225_d**).

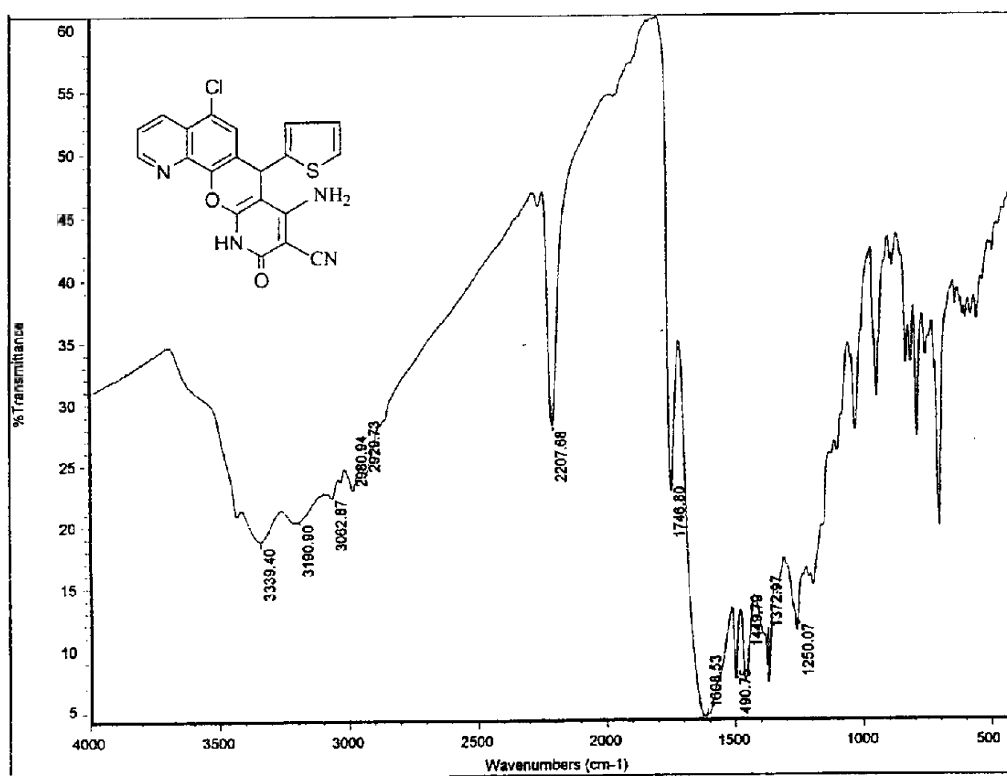


Fig.(37): 8-Amino-5-chloro-9-cyano-7-thienyl-7H-10-oxo-10,11-dihydropyrido-[2',3':6,5]pyrano[3,2-h]quinoline (**225c**).

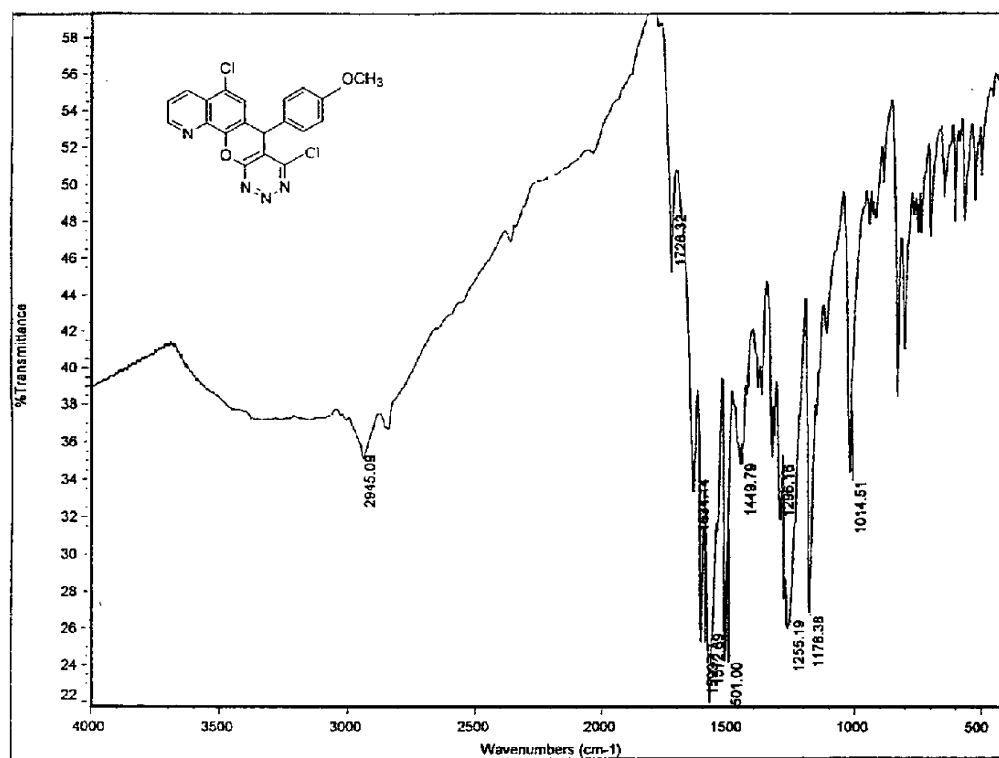


Fig.(38): 4,7-Dichloro-5-(4-methoxy)phenyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline (**226_b**).

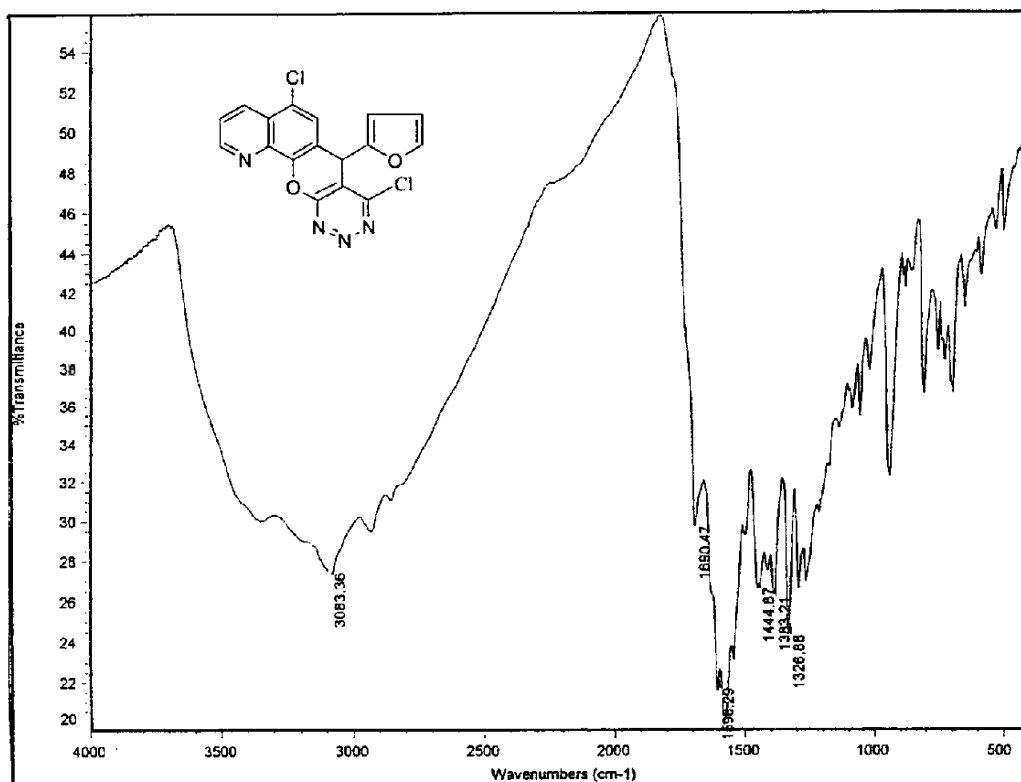


Fig.(39): 4,7-Dichloro-5-furyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline (**226_d**).

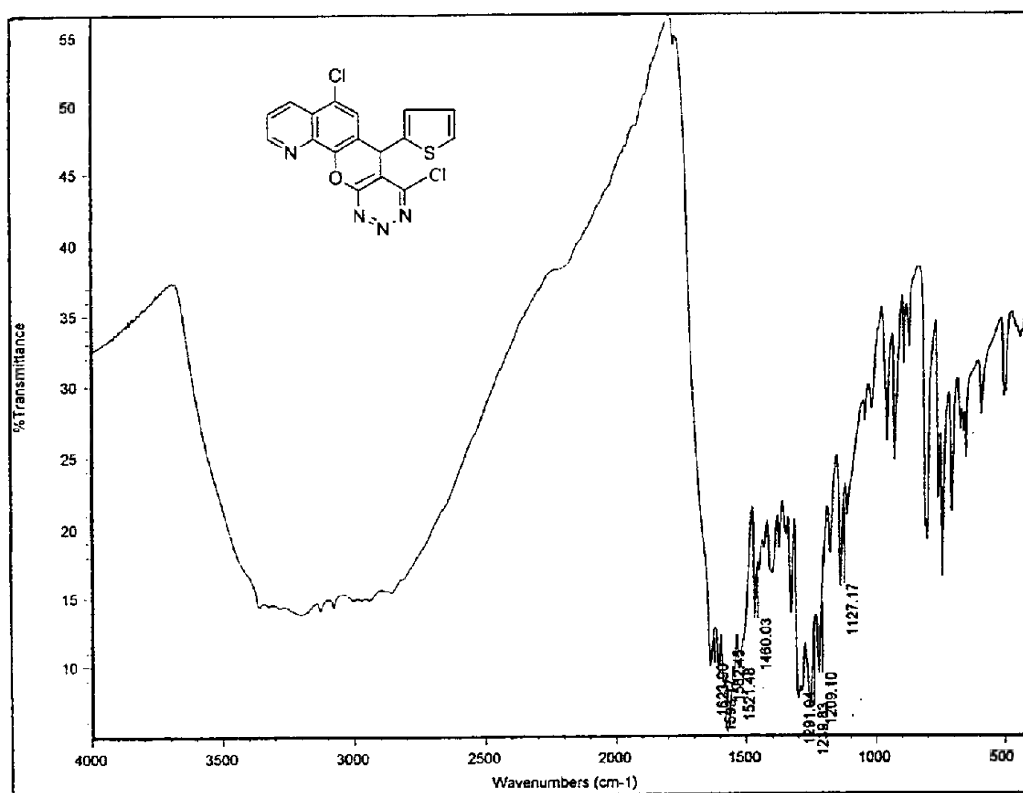


Fig.(40): 4,7-Dichloro-5-thienyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline (**226_e**)

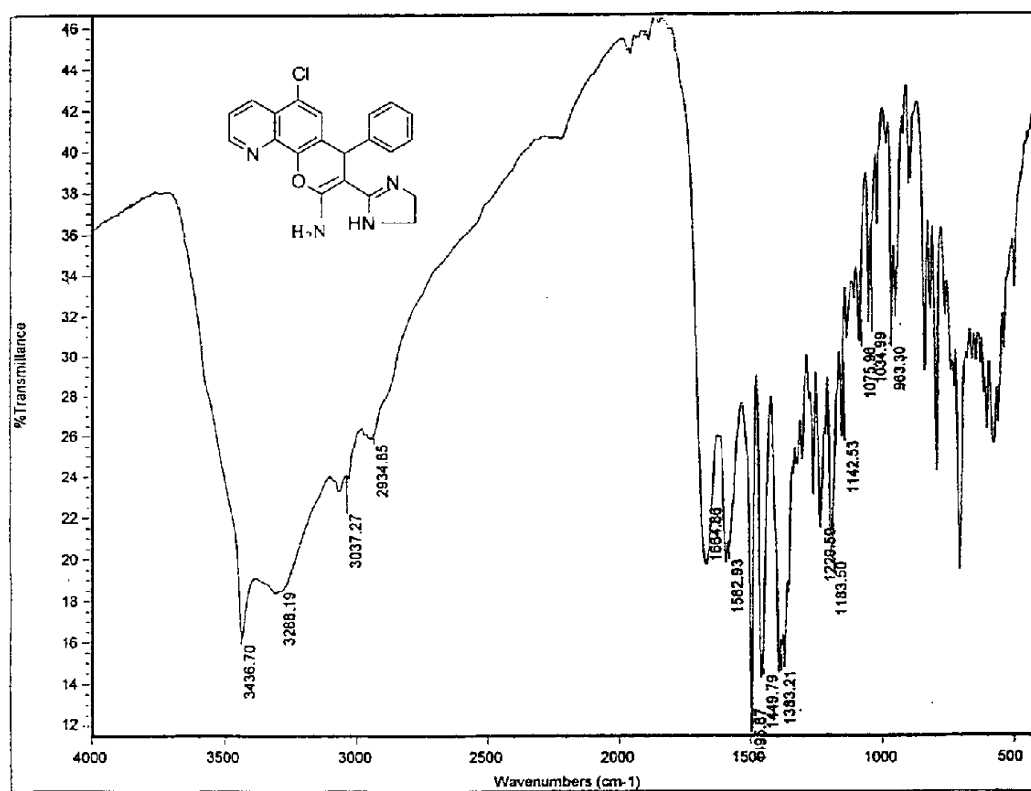
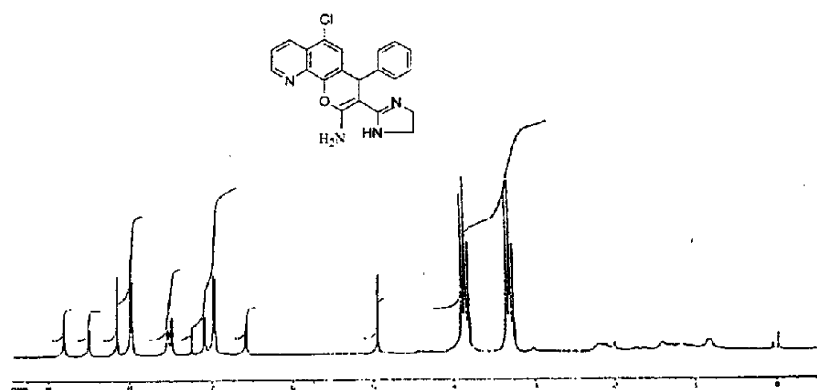


Fig.(41): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-phenyl-4H-pyrano-[3,2-h]quinoline (227_a).

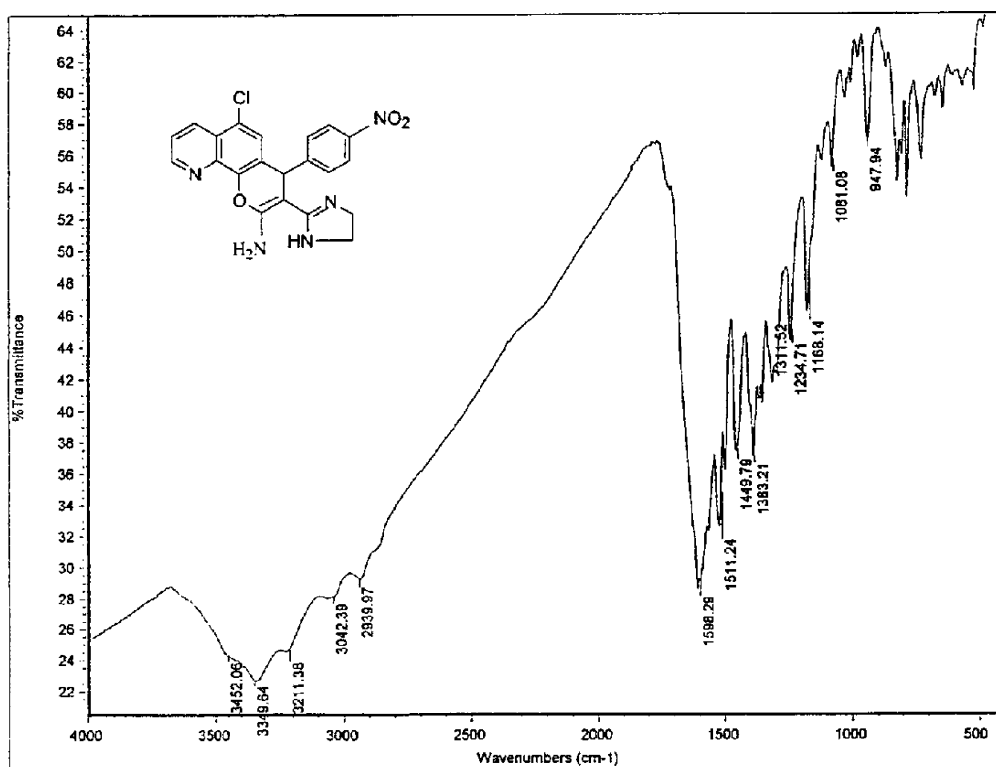


Fig.(42): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano[3,2-h]quinoline (**227c**).

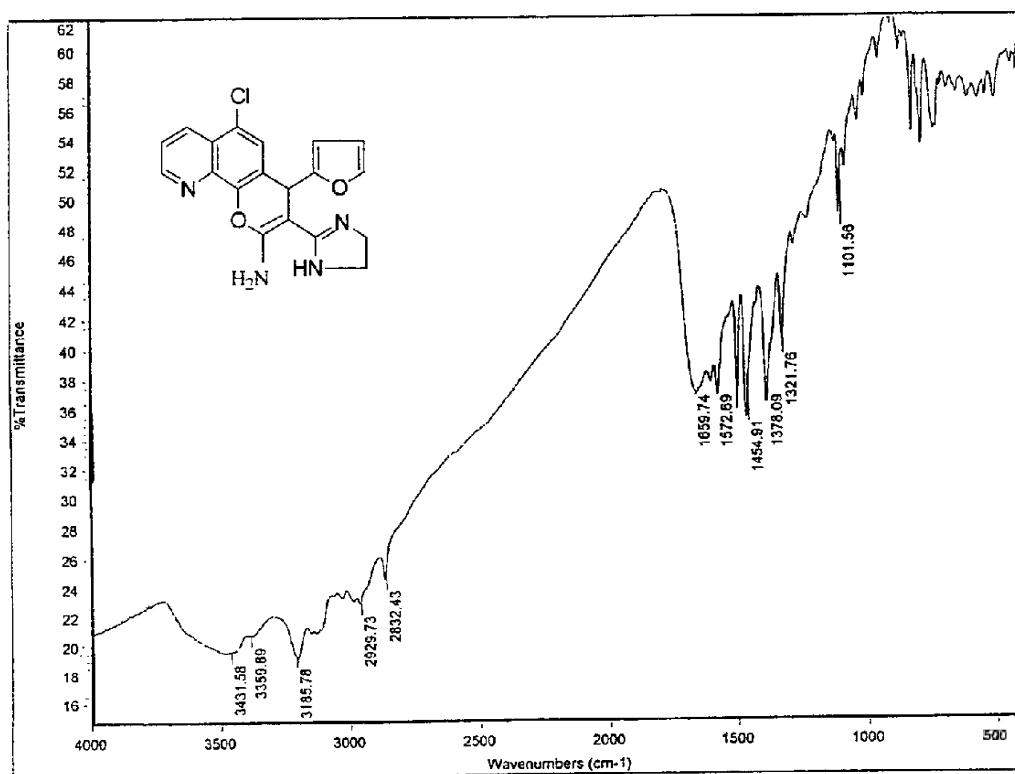


Fig.(43): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-furyl-4H-pyrano-[3.2-h]quinoline (**227_d**).

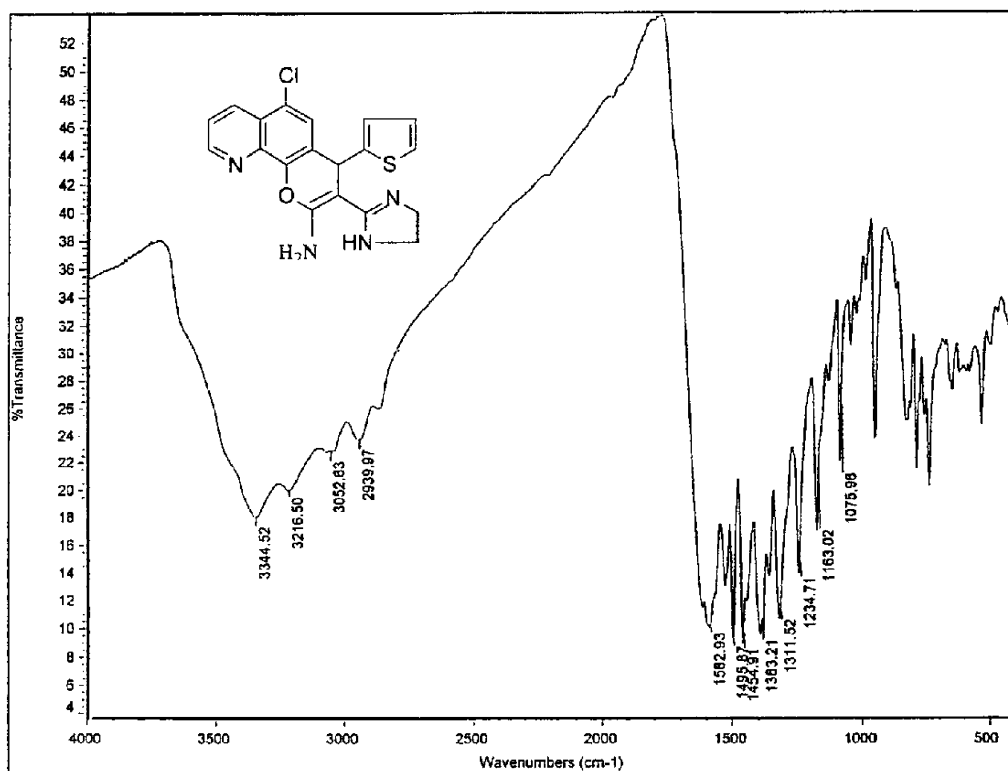


Fig.(44): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-thienyl-4H-pyrano-[3,2-h]quinoline (**227_c**).

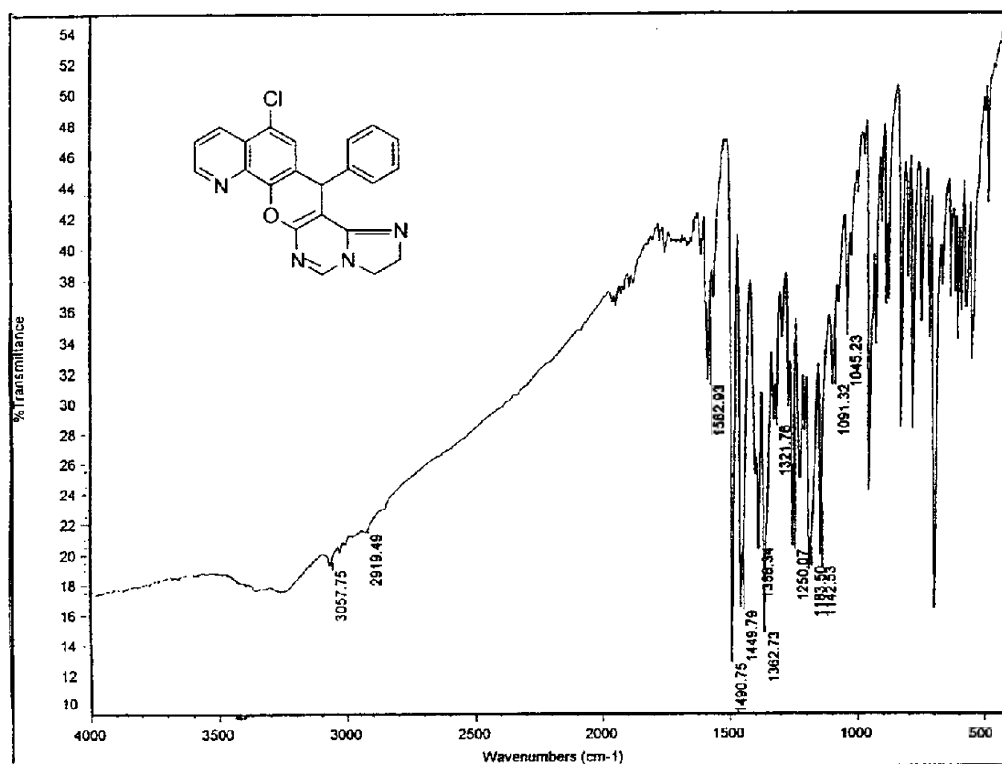


Fig.(45): 12-Chloro-14-phenyl-1,3,14-trihydroimidazo[1,2-c]pyrimido [4',5':6,5]pyrano[3,2-h]quinoline (228_a).

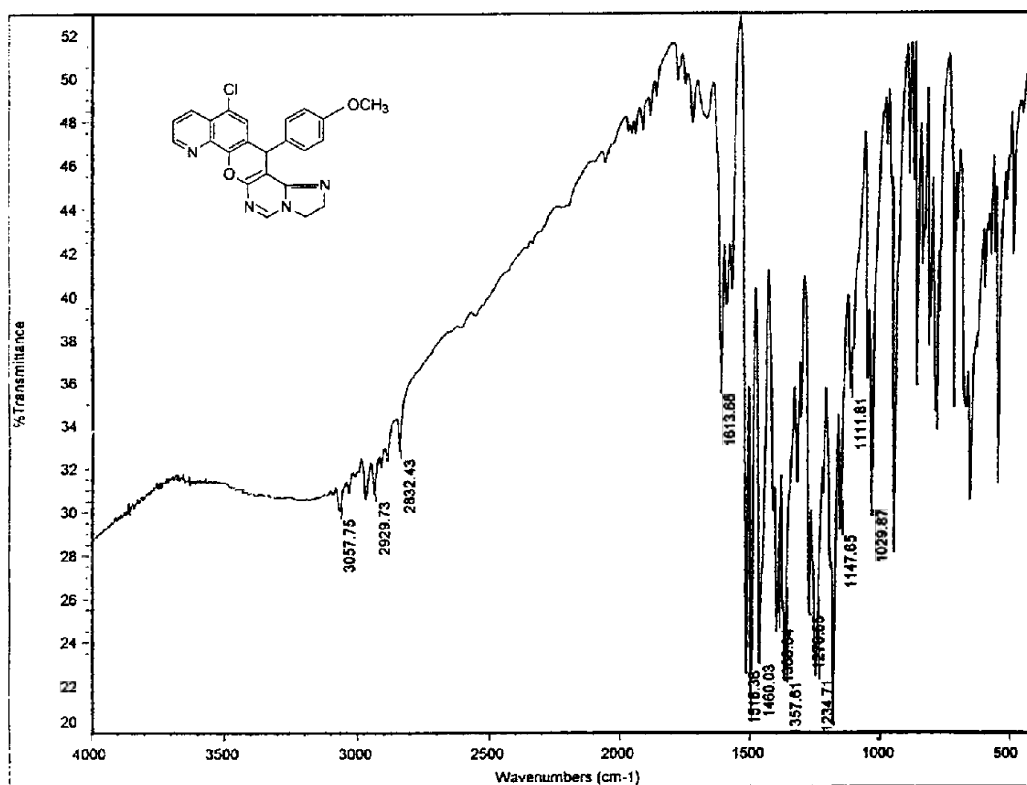


Fig.(46): 12-Chloro-14-(4-methoxy)phenyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (228_b).

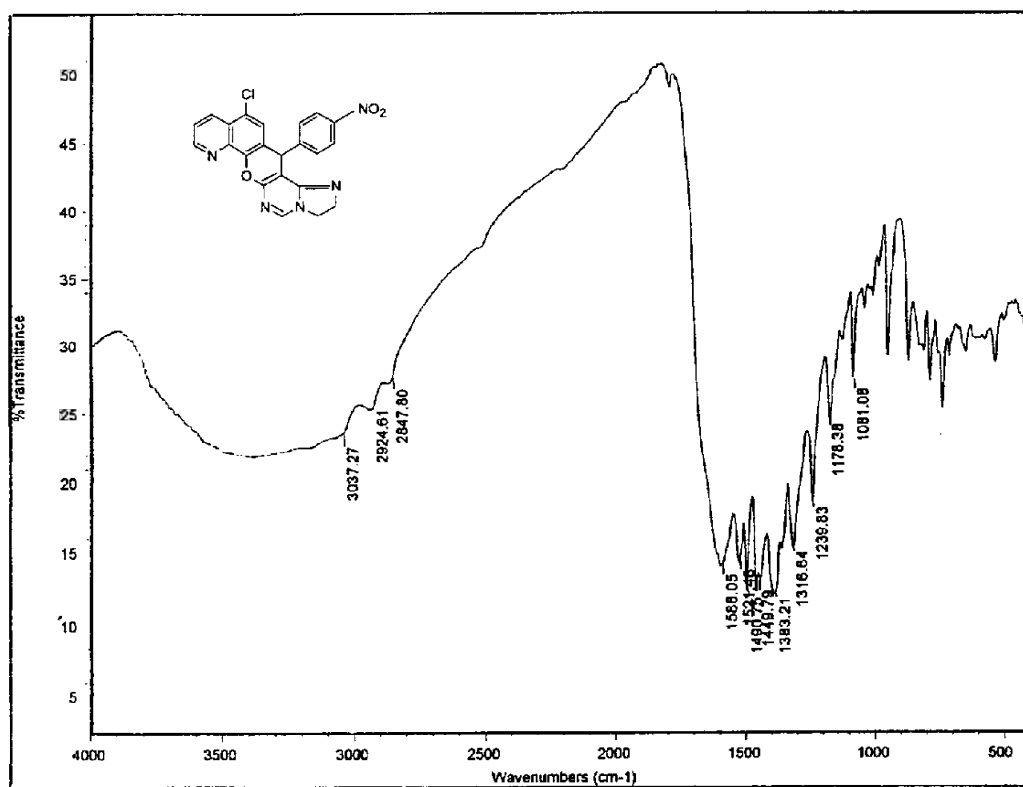


Fig.(47): 12-Chloro-14-(4-nitro)phenyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**228_c**).

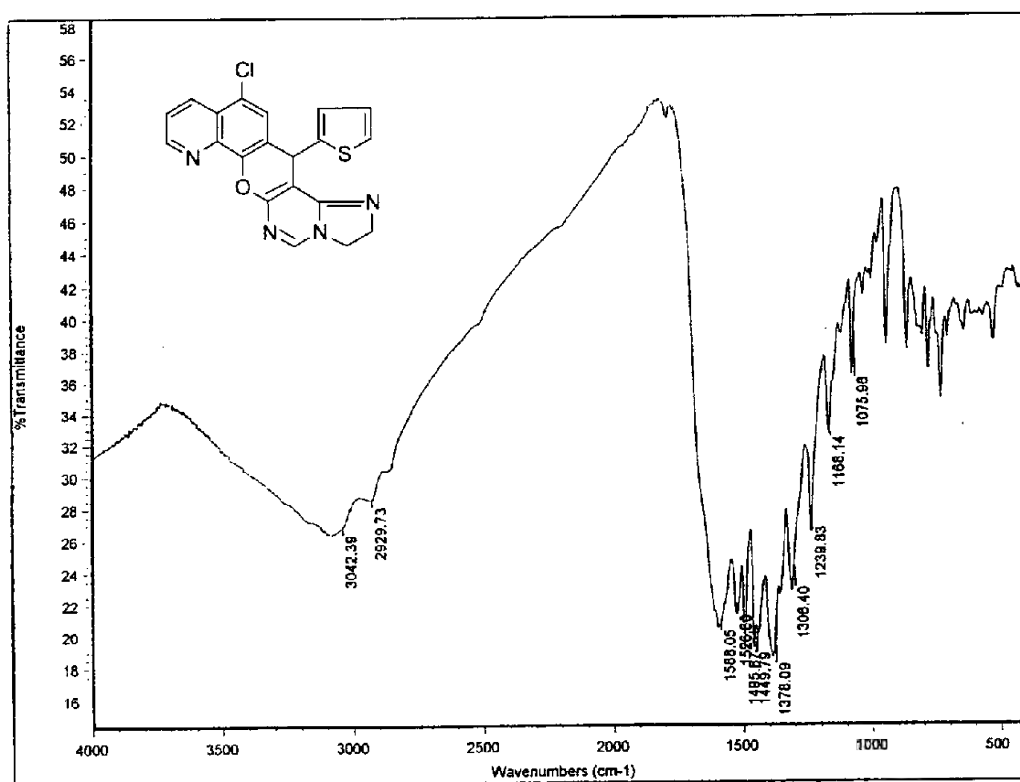


Fig.(48): 12-Chloro-14-thienyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**228_c**).

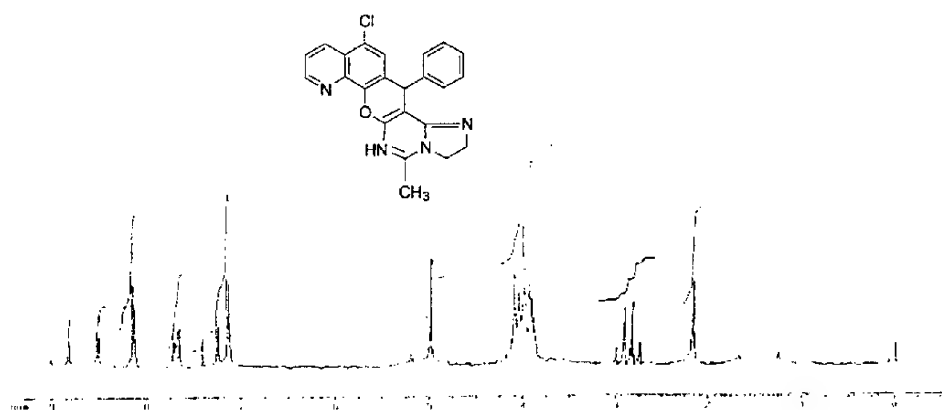


Fig.(49): 12-Chloro-5-methyl-14-phenyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**229_a**).

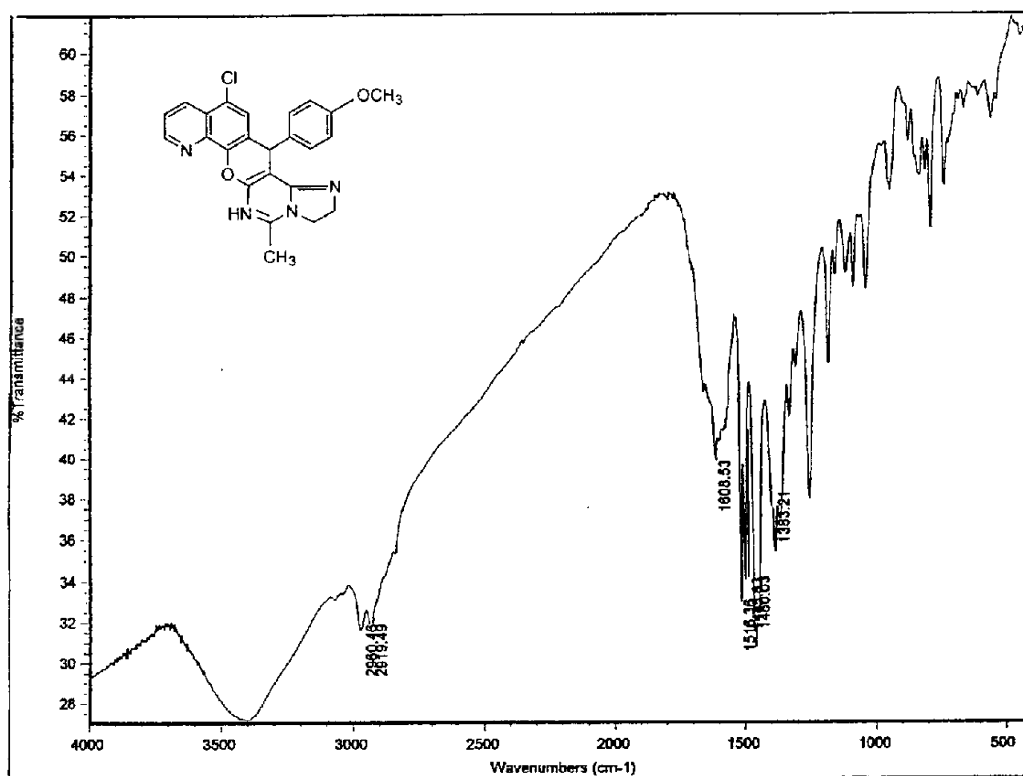


Fig.(50): 12-Chloro-5-methyl-14-(4-methoxy)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**229_b**).

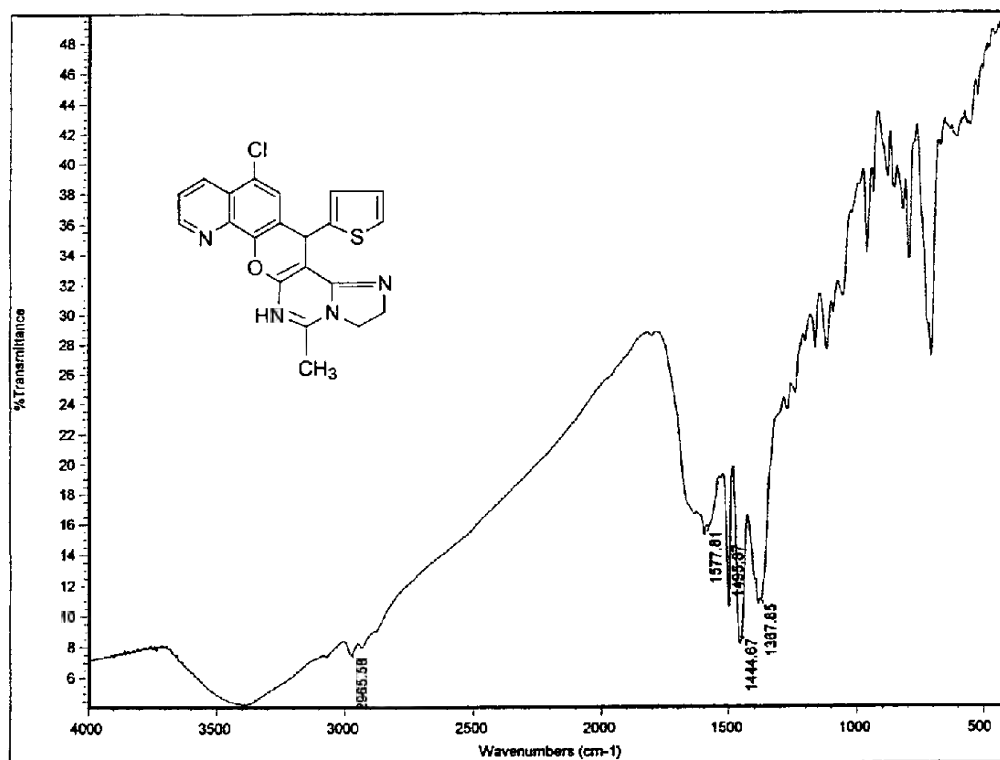


Fig.(51): 12-Chloro-5-methyl-14-thienyl-2,3,5,6,14- pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**229_e**).

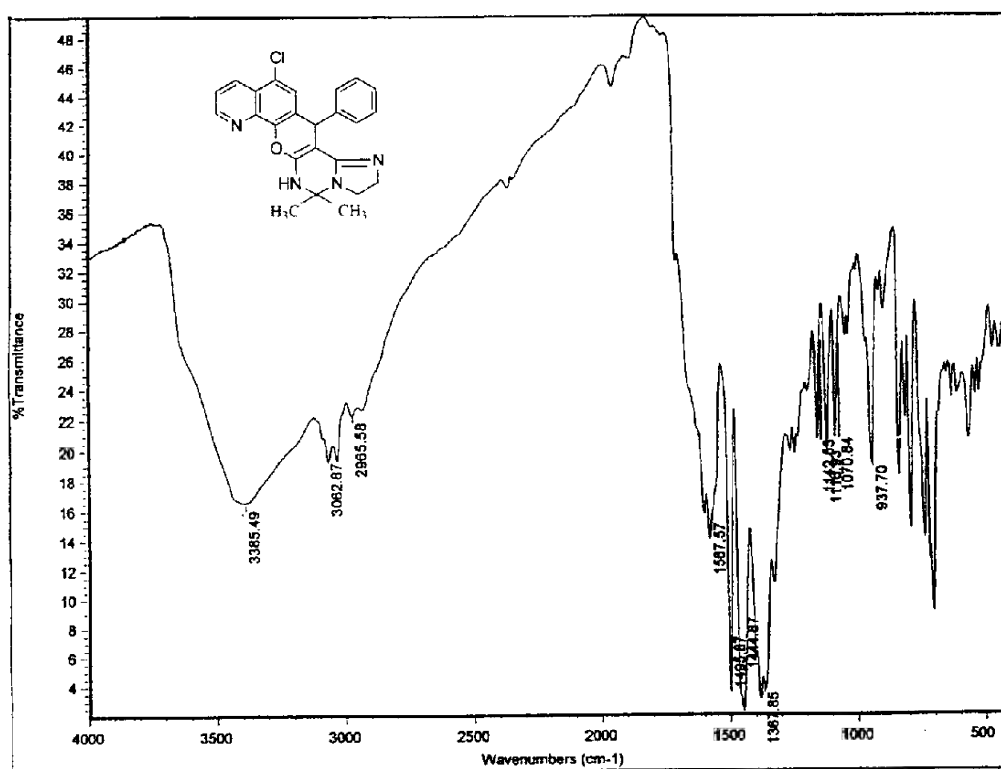
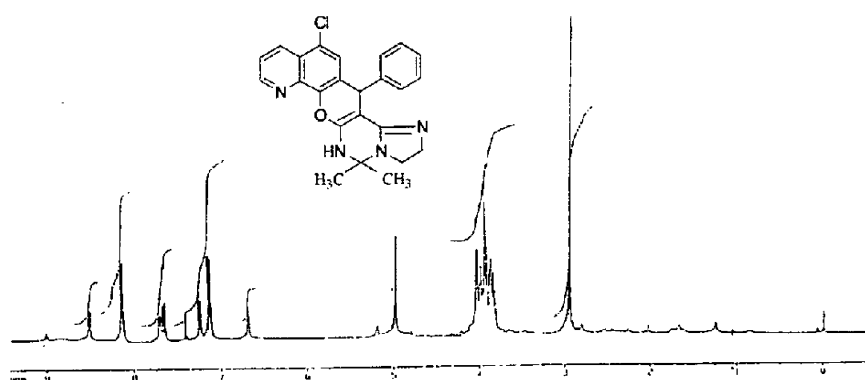


Fig.(52): 12-Chloro-5,5-dimethyl-14-phenyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230_a**).

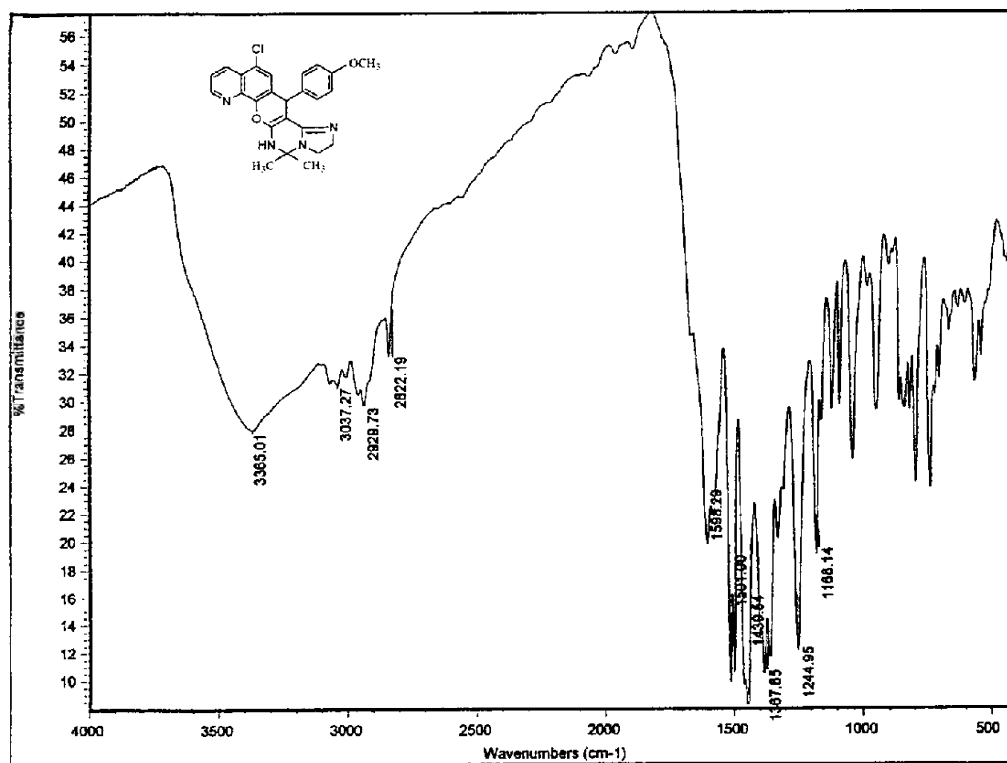


Fig.(53): 12-Chloro-5,5-dimethyl-14-(4-methoxy)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230_b**).

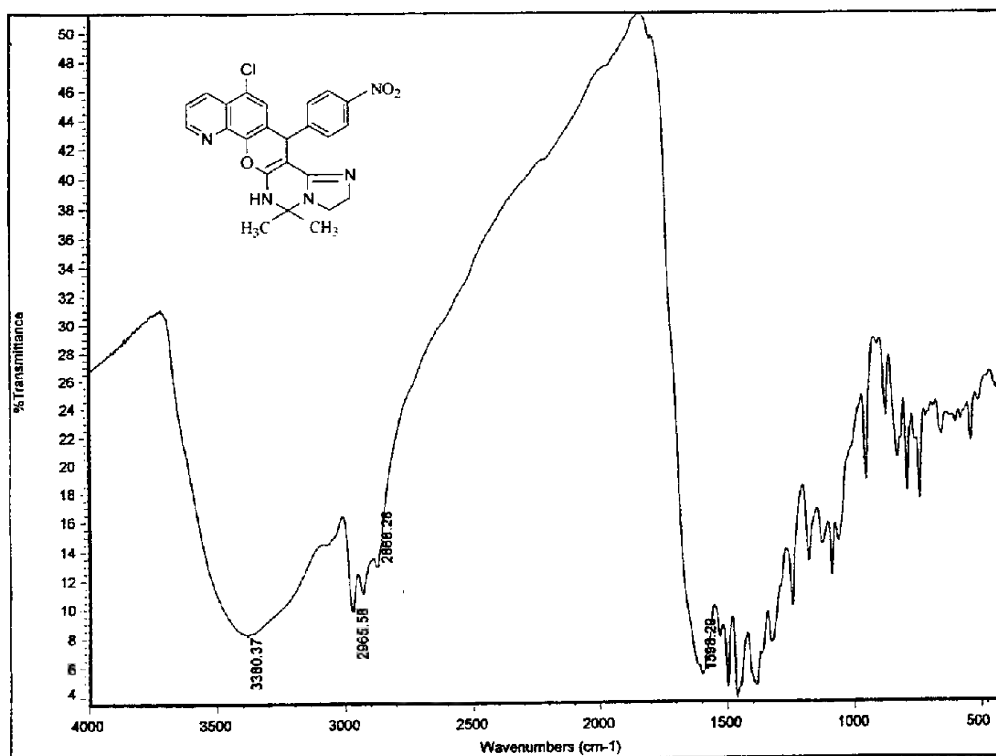


Fig.(54): 12-Chloro-5,5-dimethyl-14-(4-nitro)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230_c**).

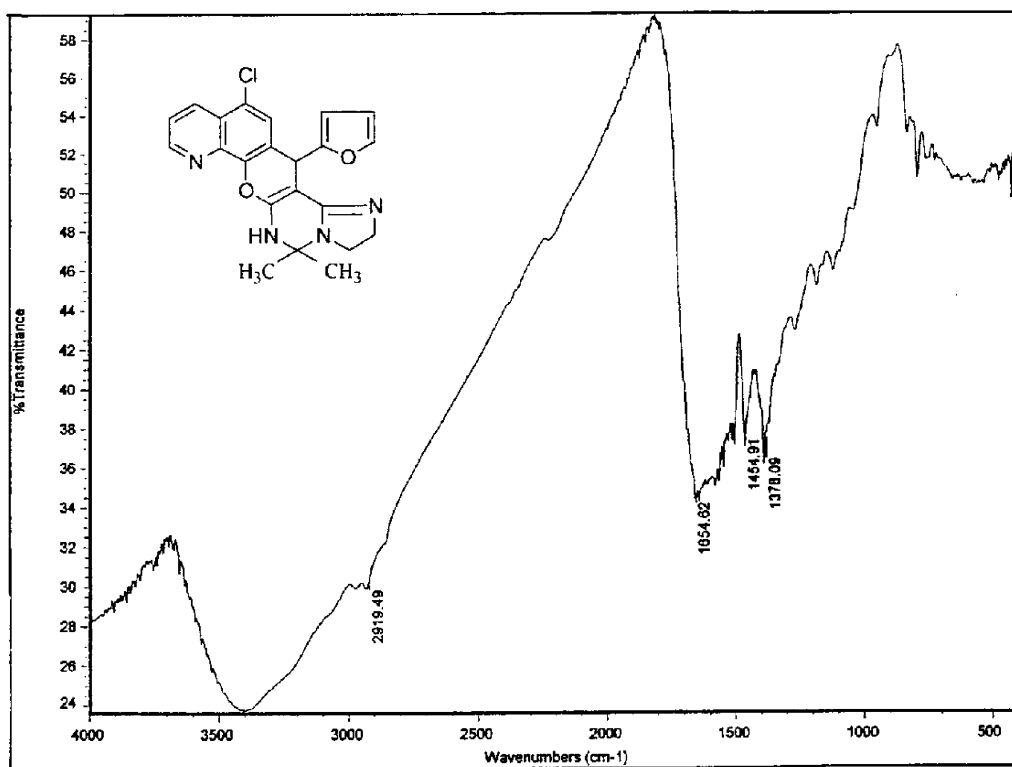


Fig.(55): 12-Chloro-5,5-dimethyl-14-furyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230_a**).

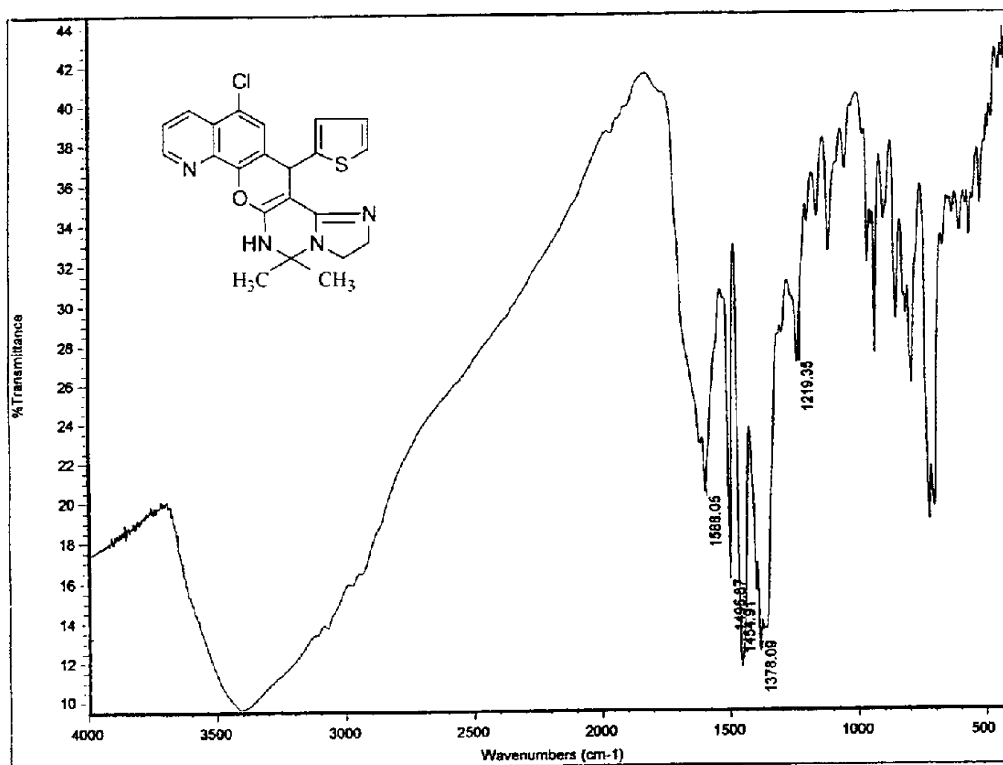


Fig.(56): 12-Chloro-5,5-dimethyl-14-thienyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230_e**).

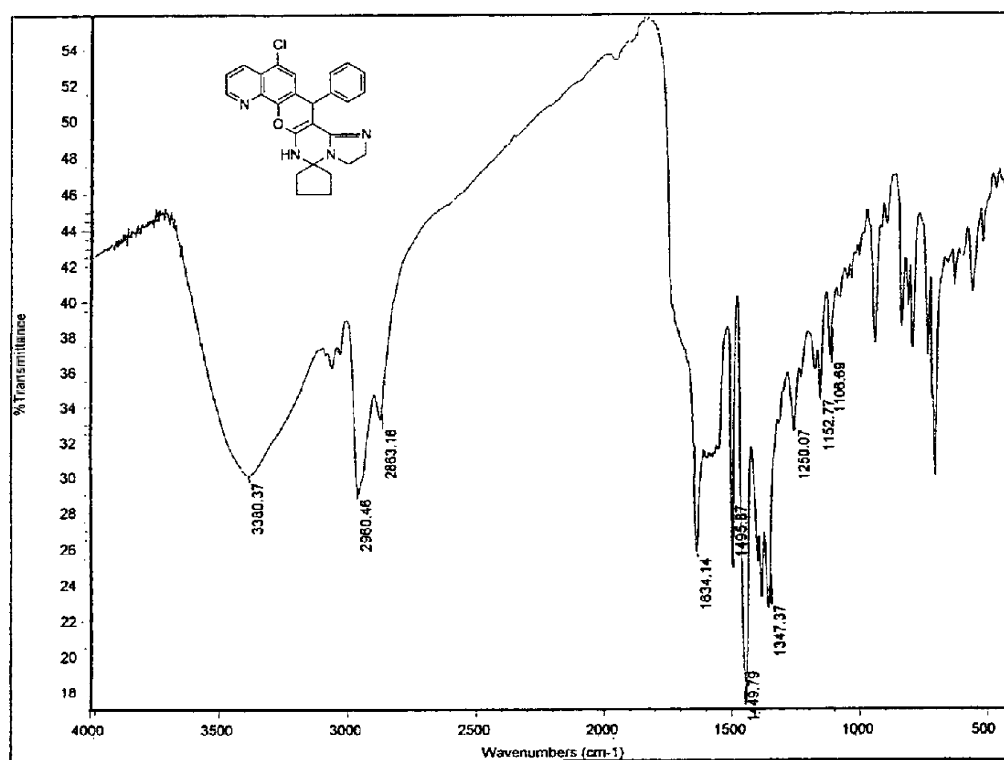


Fig.(57): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-spiro(1'-cycloheptane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**231_a**).

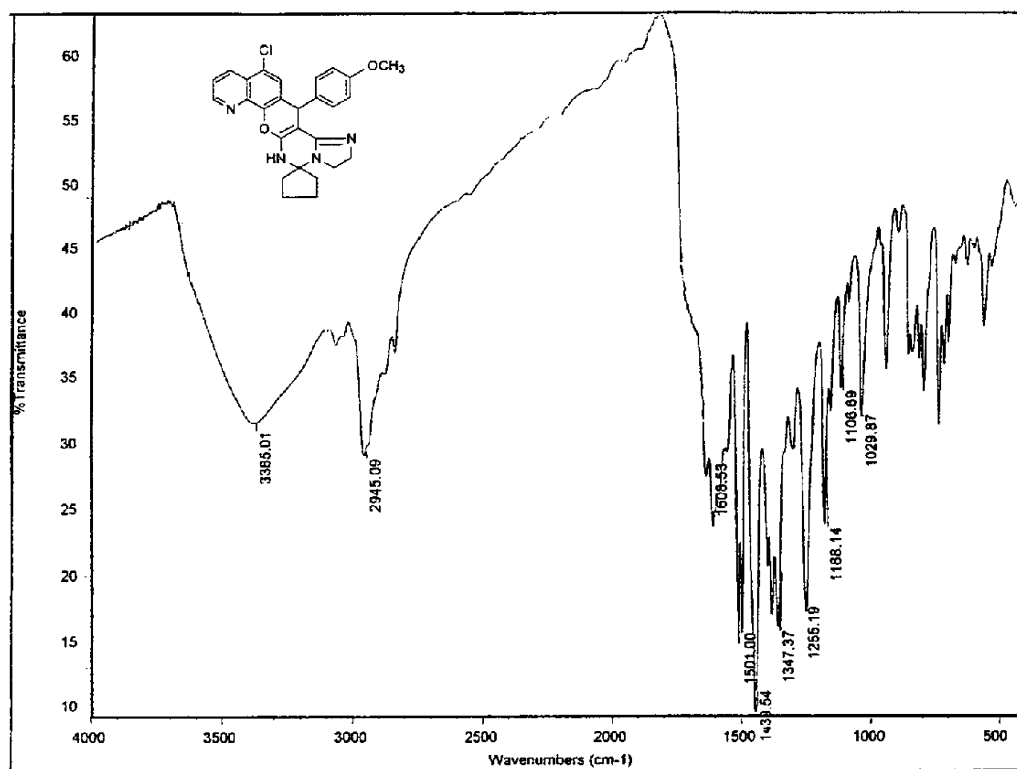


Fig.(58): 12-Chloro-14-(4-methoxy)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclopentane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (231_b).

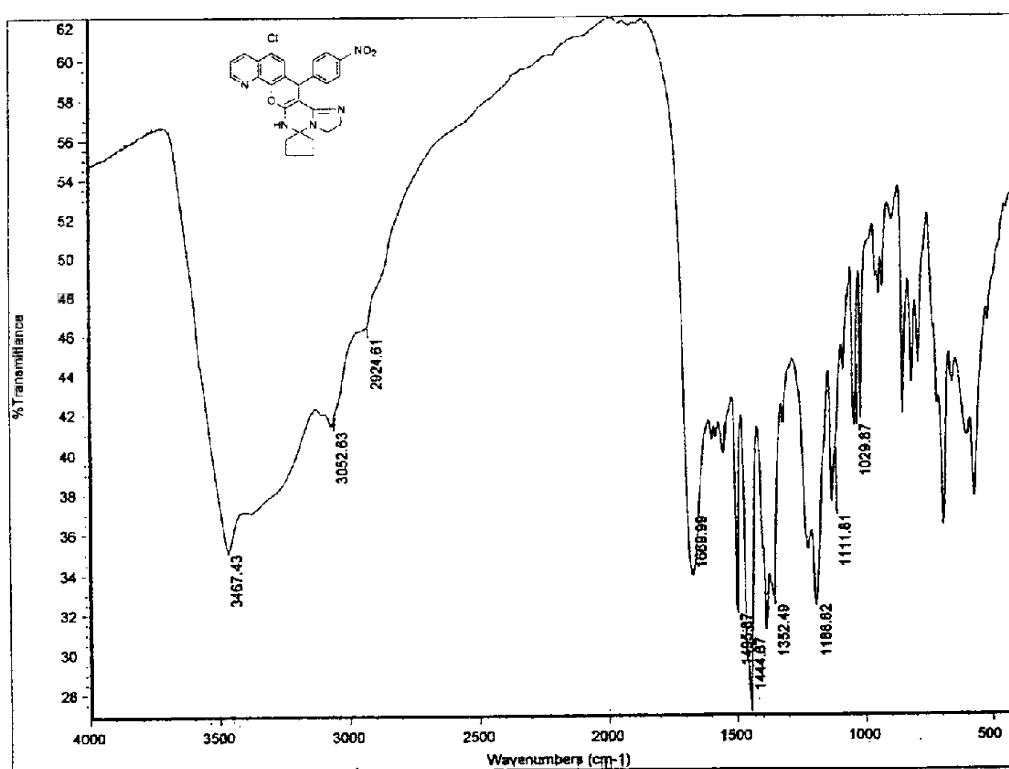
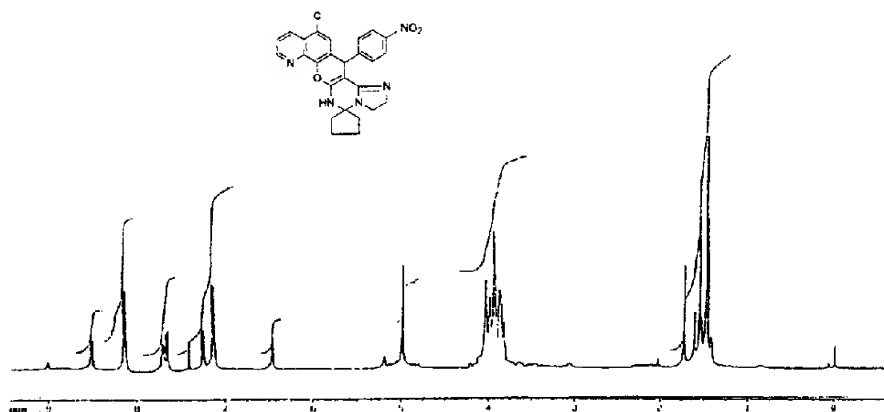


Fig.(59): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclopentane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (231_c).

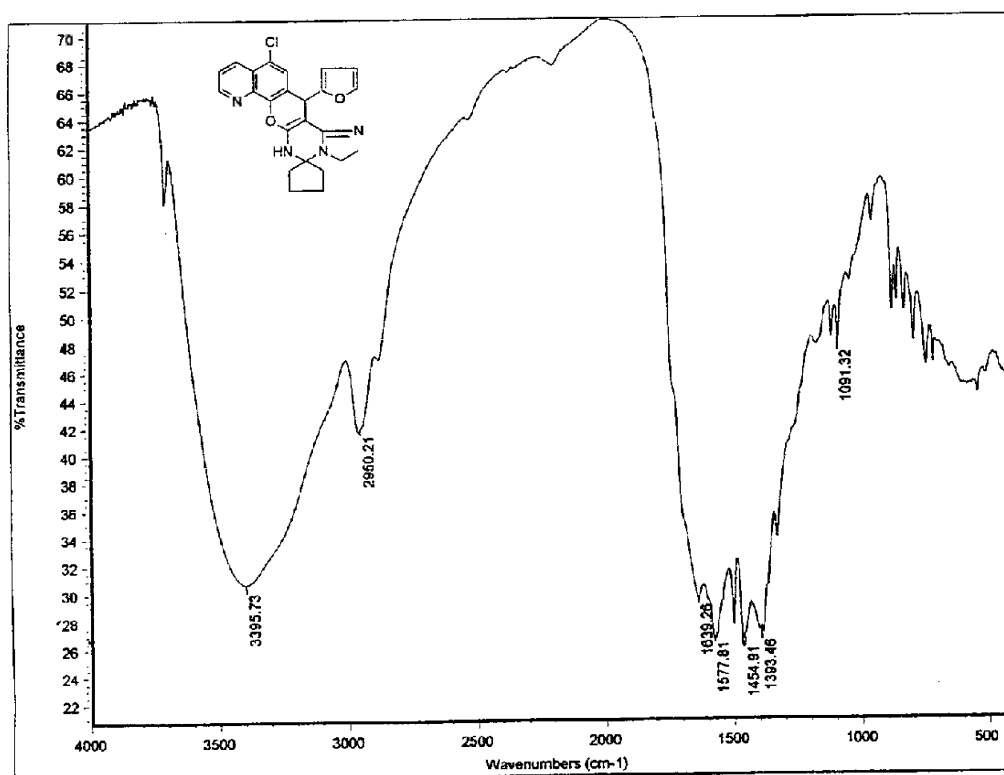


Fig.(60): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclopentane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**231_d**).

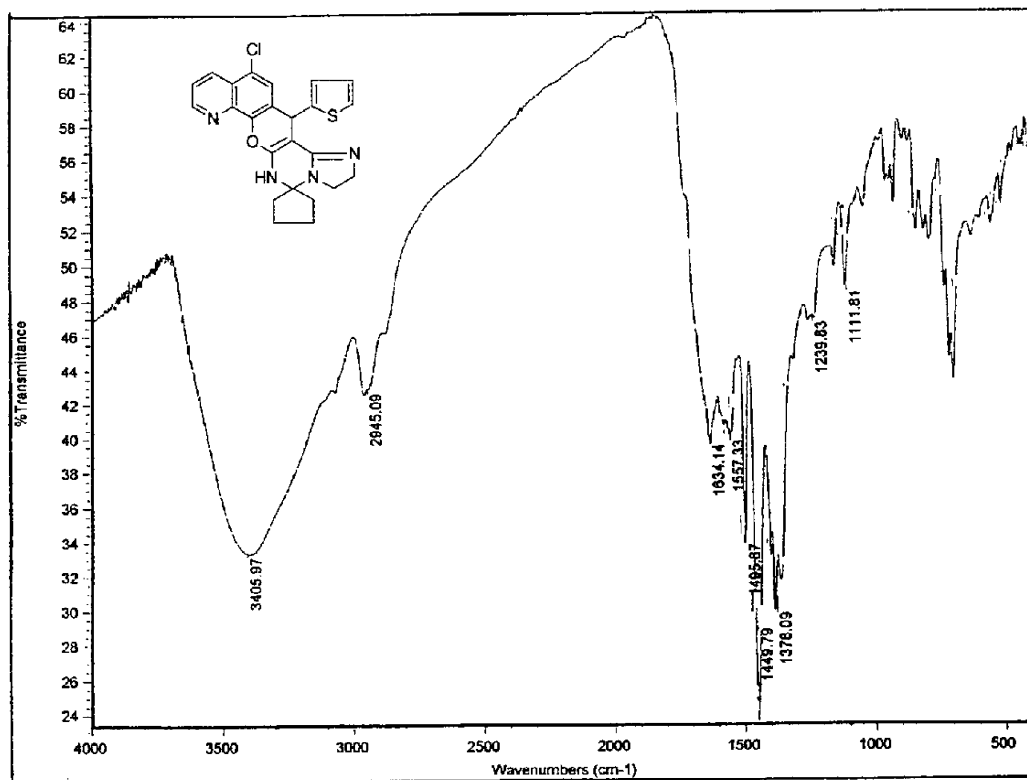


Fig.(61): 12-Chloro-14-thienyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclopentane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**231c**).

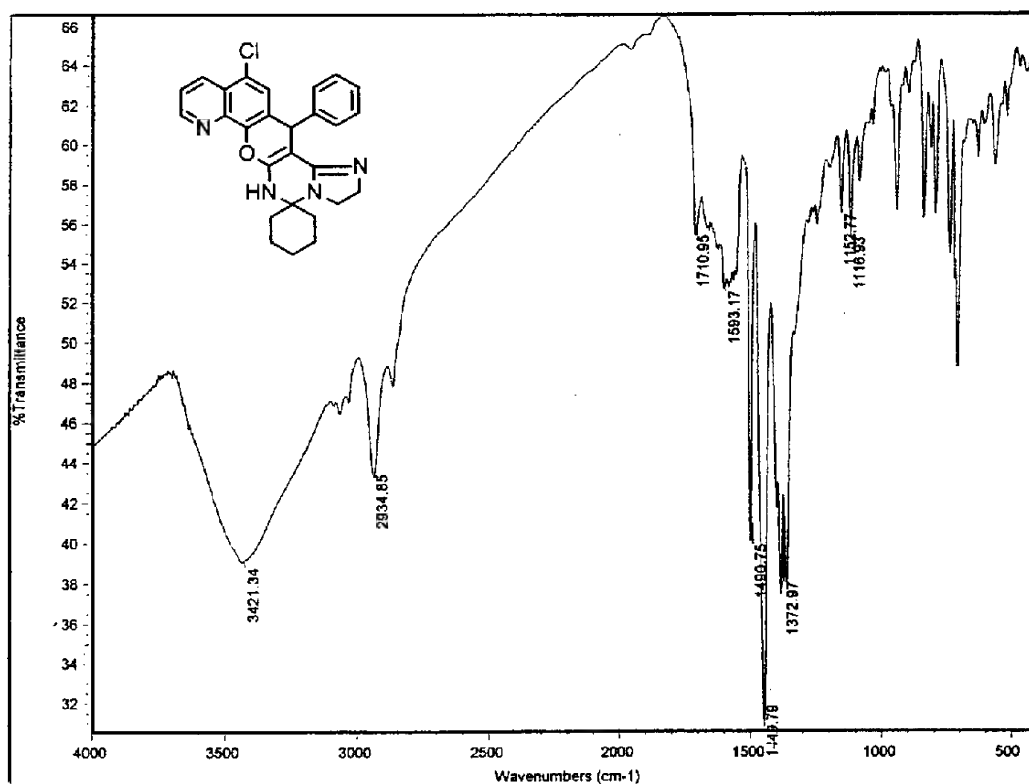


Fig.(62): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**232_a**).

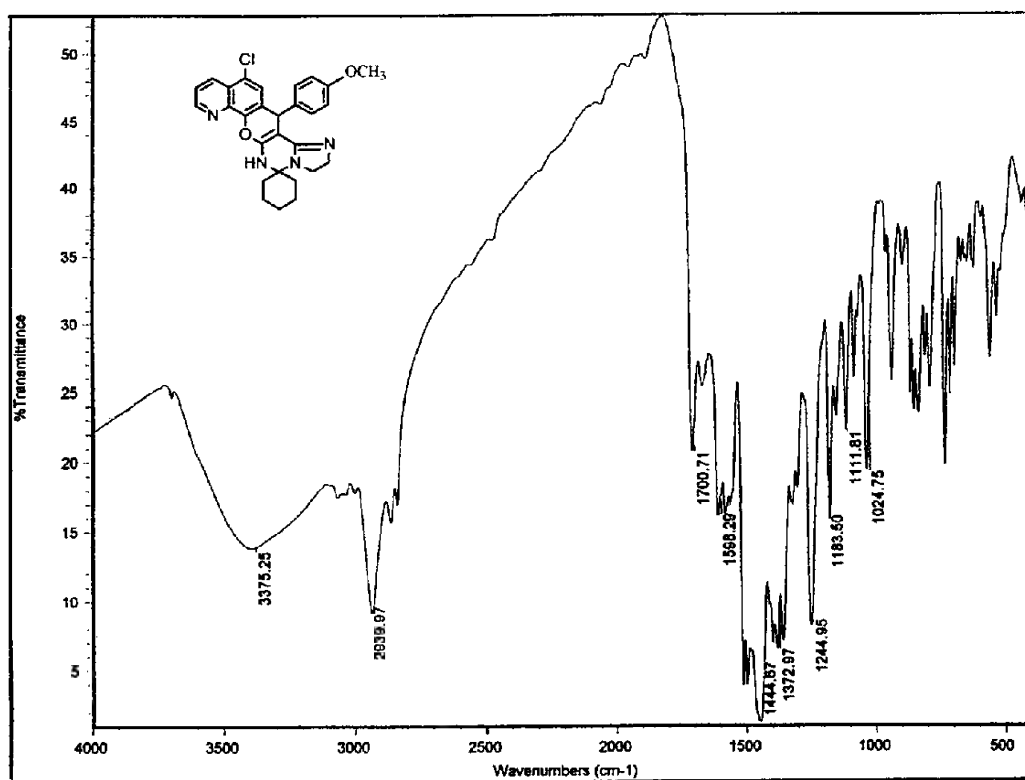


Fig.(63): 12-Chloro-14-(4-methoxy)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclohexane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (232_b).

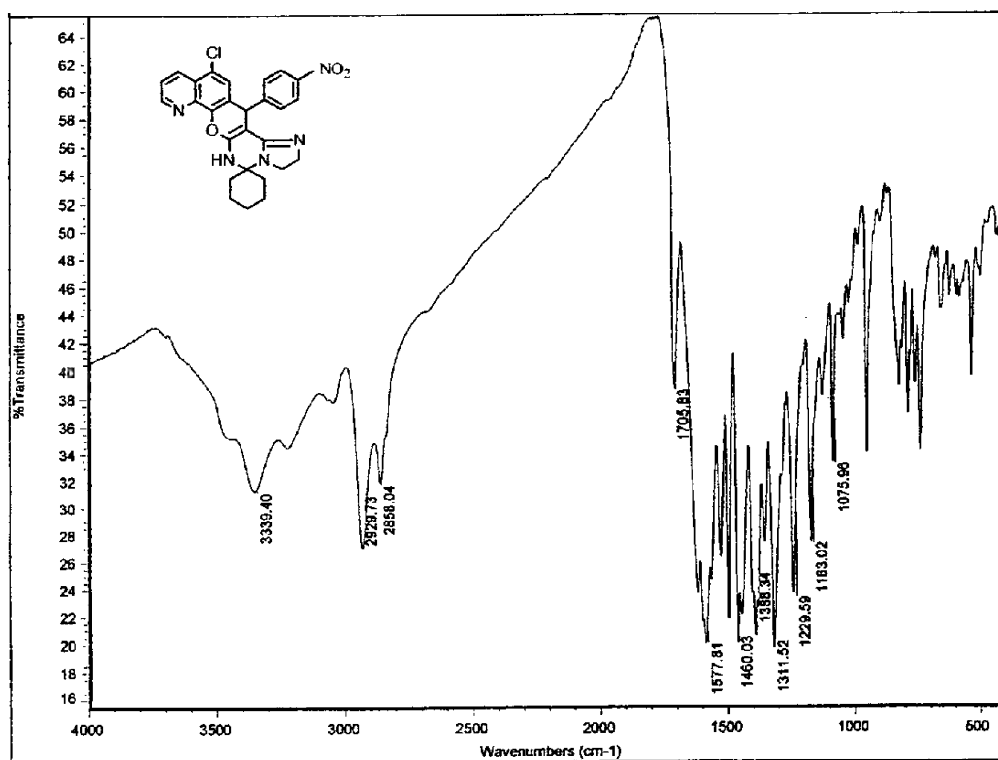


Fig.(64): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclohexane)imidazo[1,2-c]pyrimido[4,5:6,5]pyrano[3,2-h]quinoline (232_c).

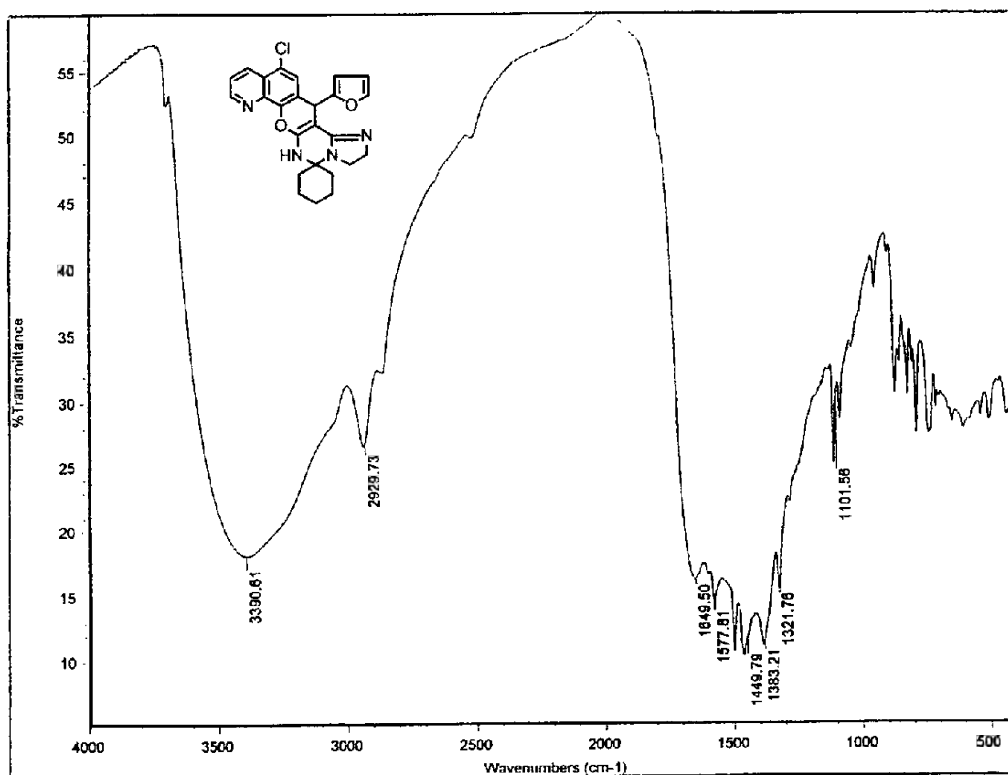


Fig.(65): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**232_d**).

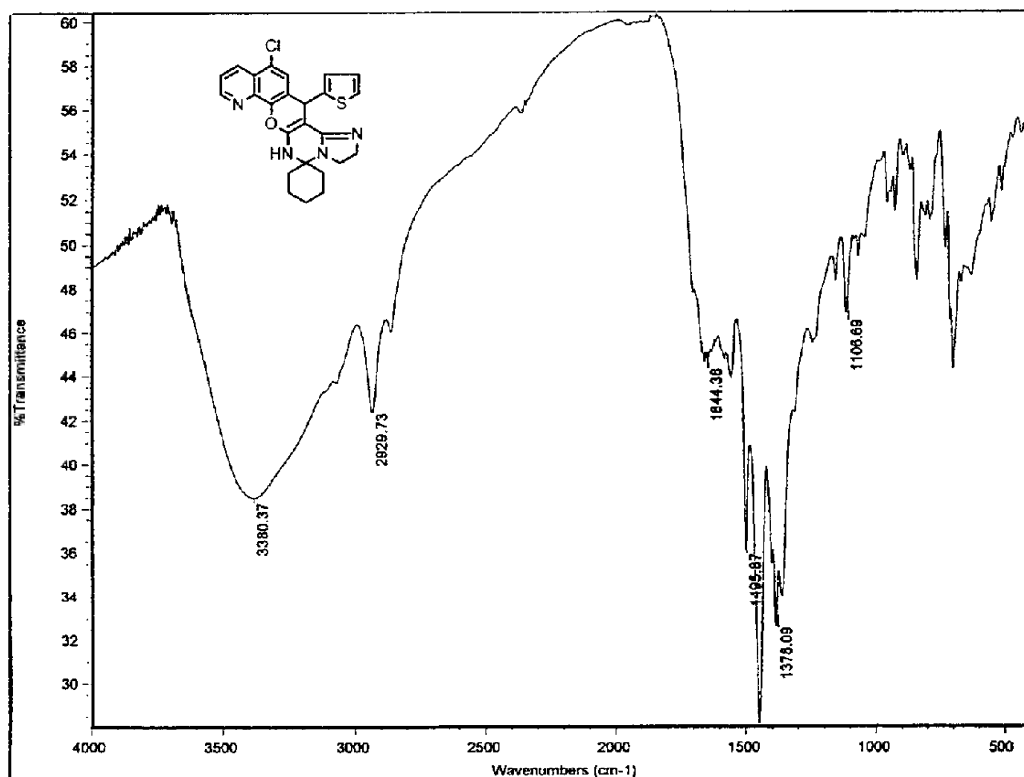


Fig.(66): 12-Chloro-14-thieryl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**232_e**).

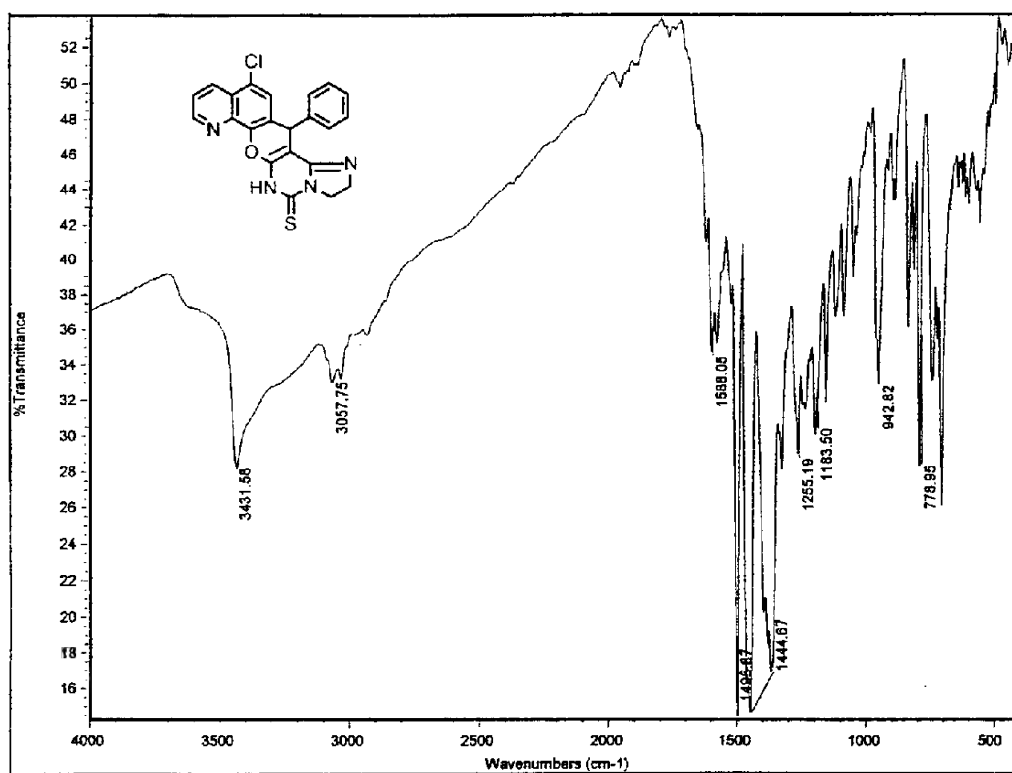
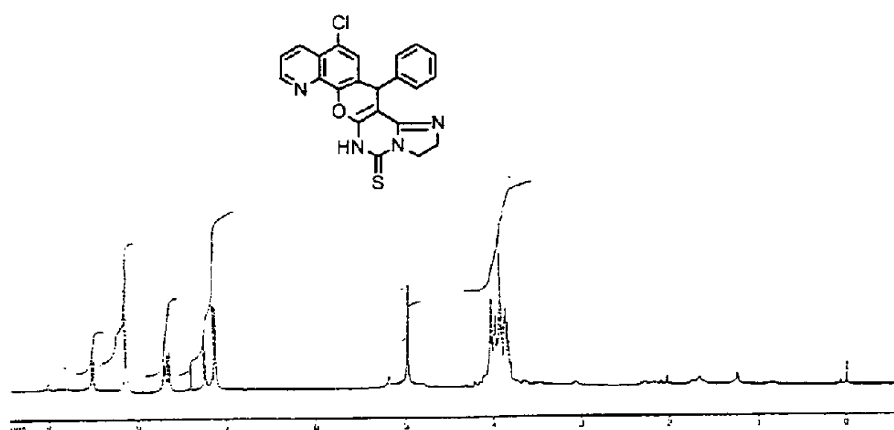


Fig.(67): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (233_a).

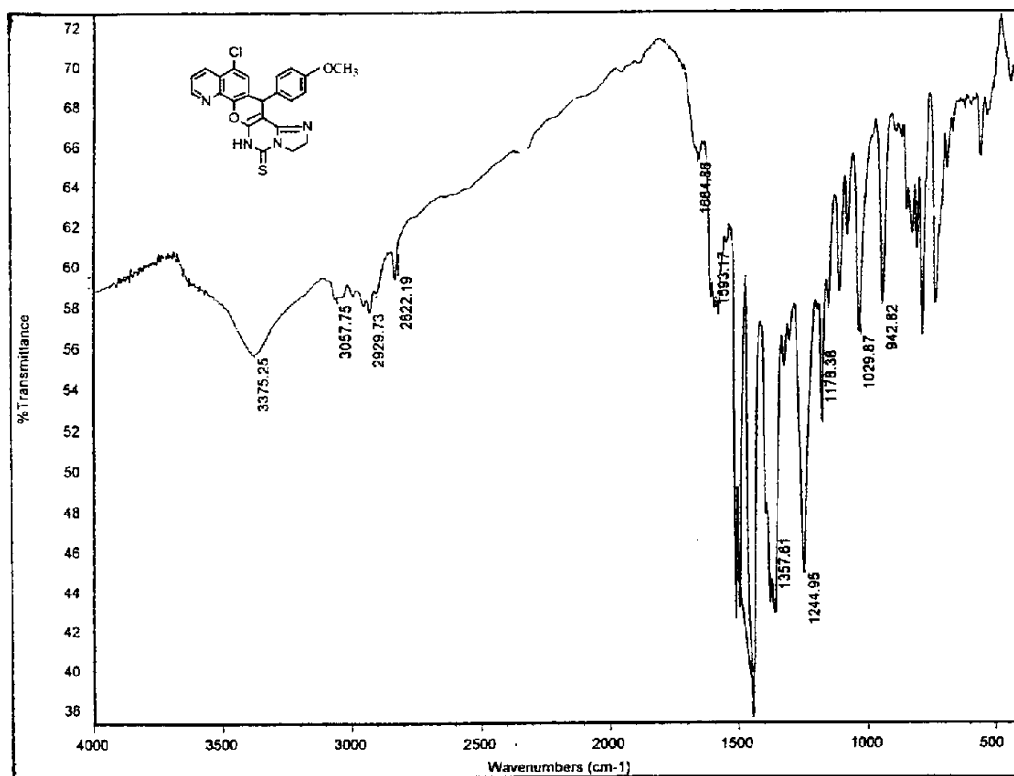


Fig.(68): 12-Chloro-14-(4-methoxy)phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (233_b).

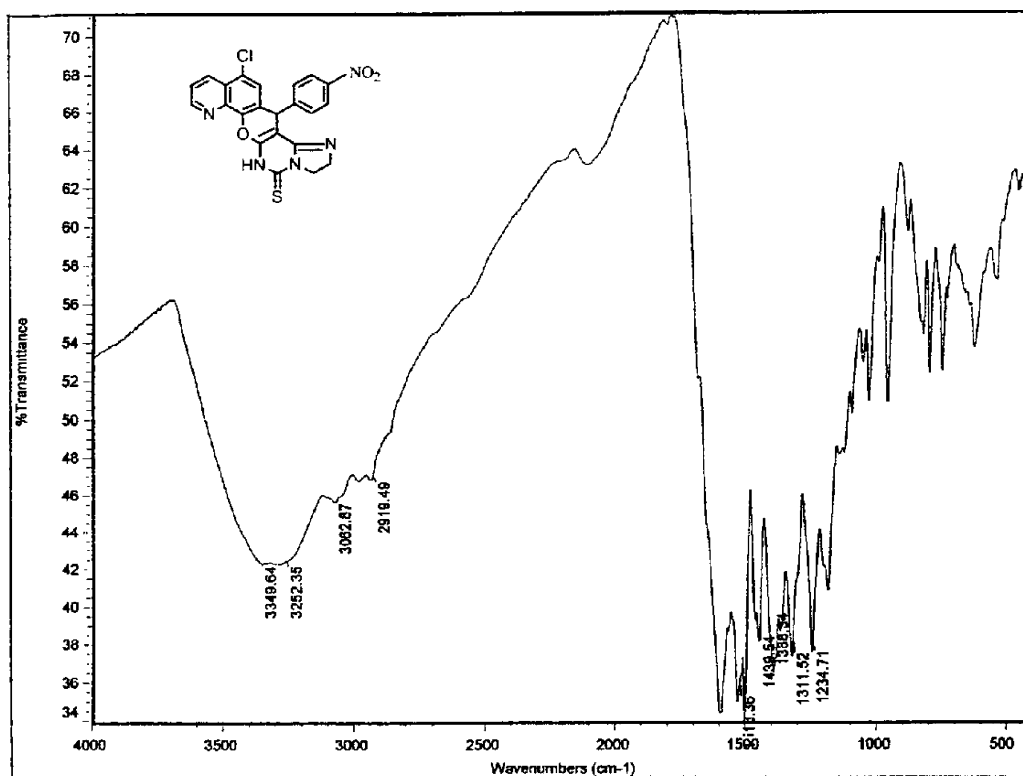


Fig.(69): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**233c**).

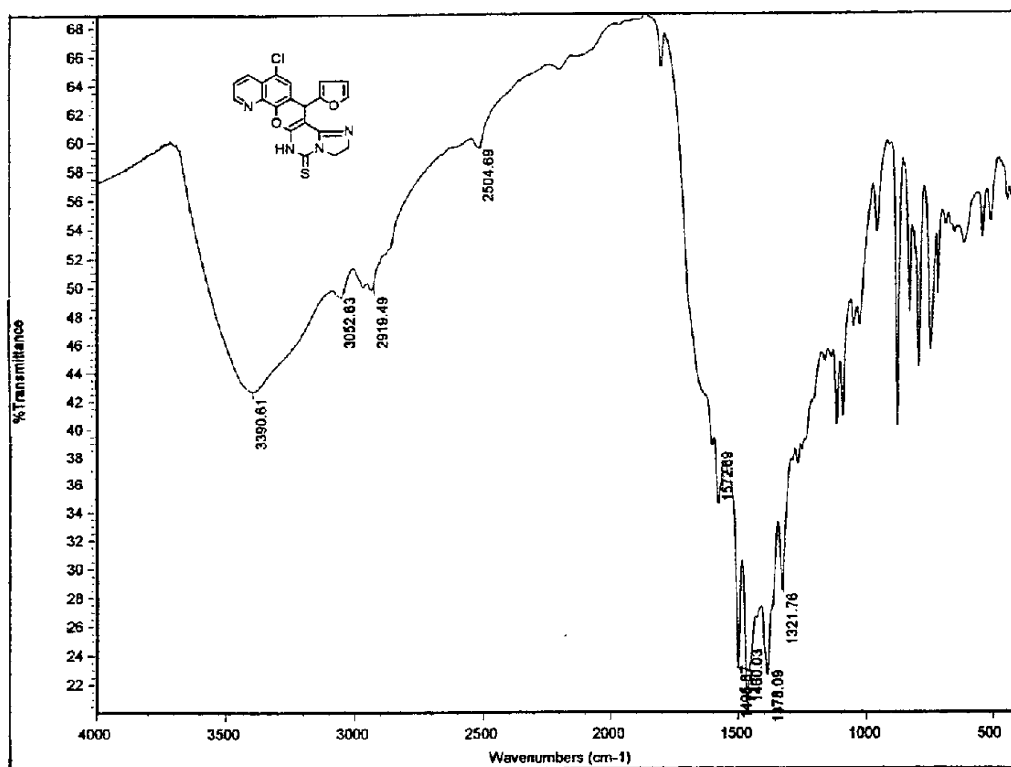


Fig.(70): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**233_d**).

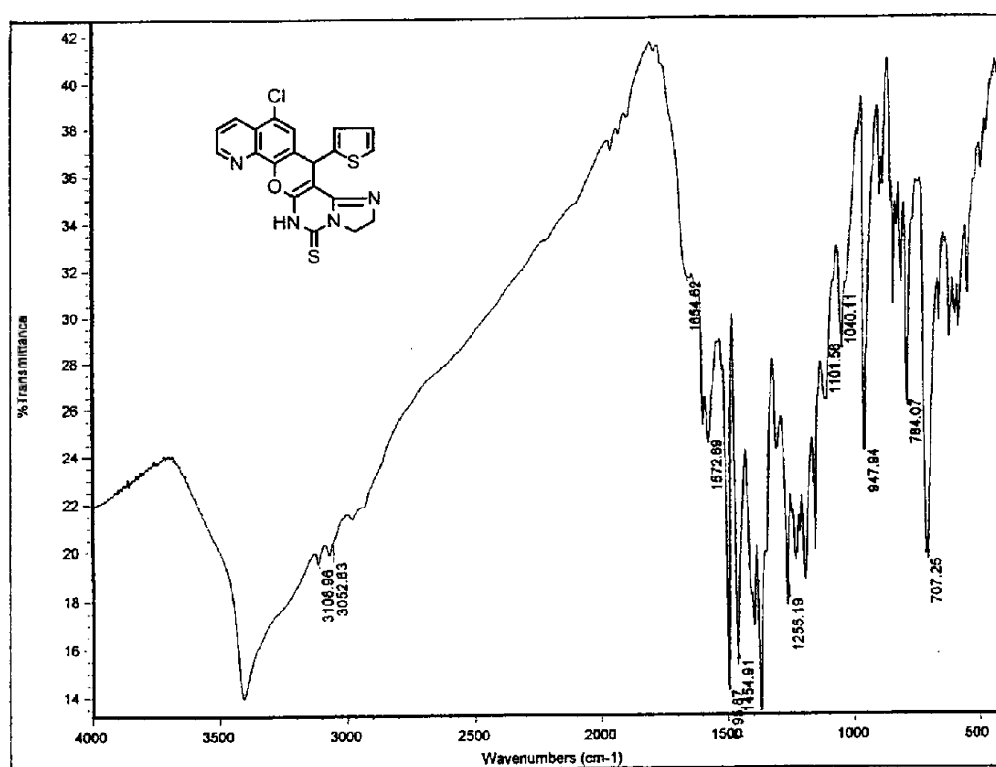


Fig.(71): 12-Chloro-14-thienyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**233_e**).

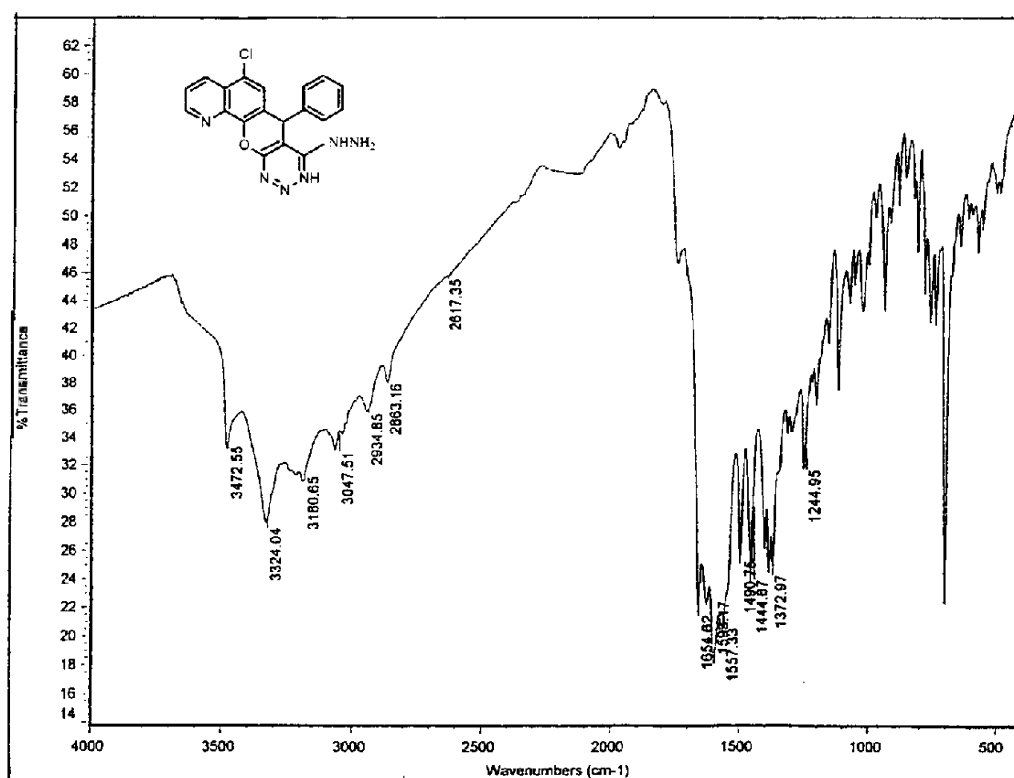
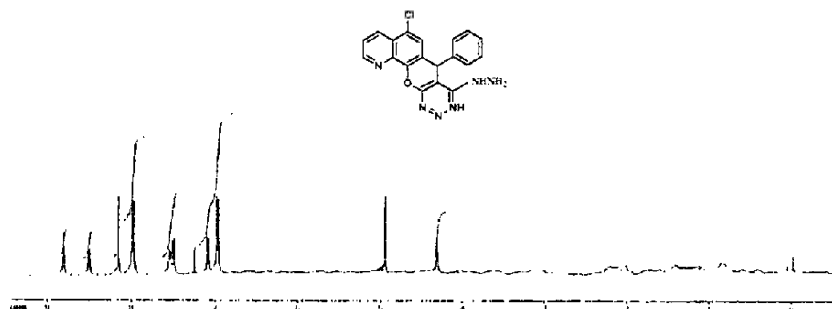


Fig.(72): 7-Chloro-5-phenyl-5H-4-hydrazino-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline (**234_a**).

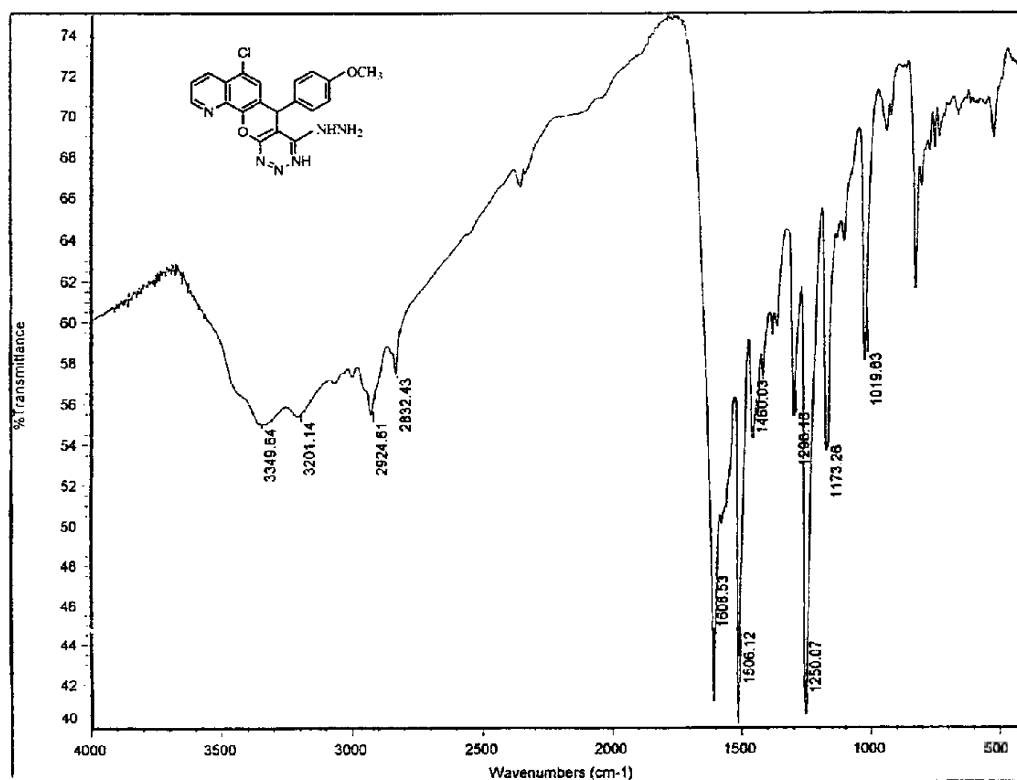


Fig.(73): 7-Chloro-5-(4-methoxy)phenyl-5H-4-hydrazino-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline (**234b**).

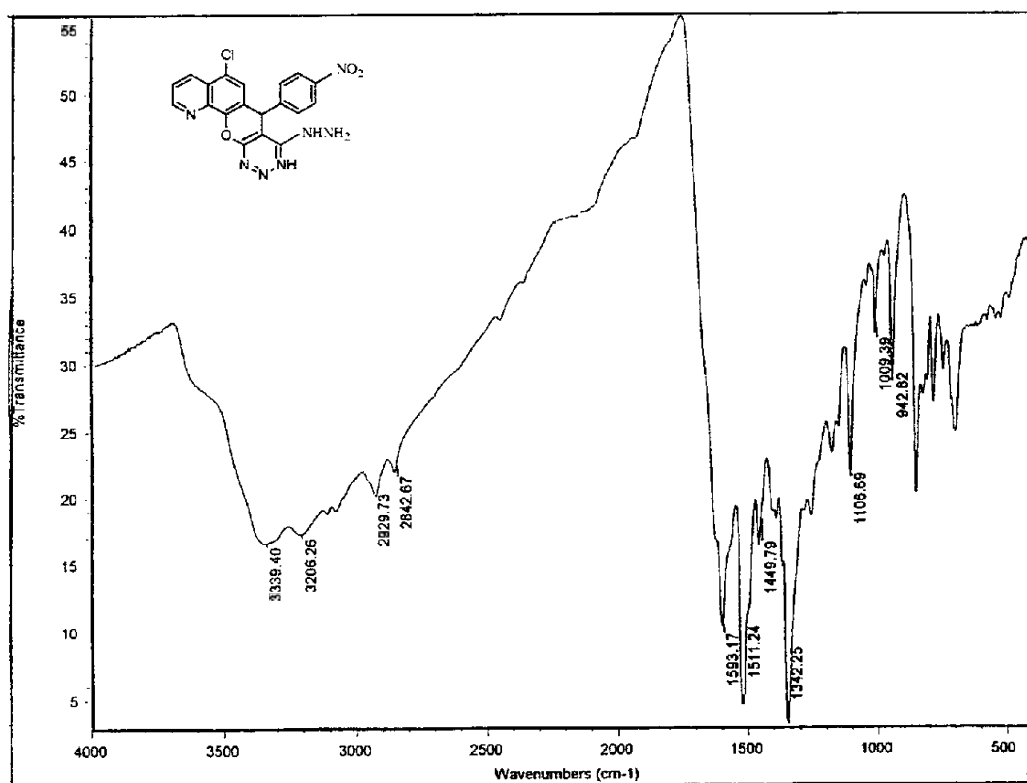


Fig.(74): 7-Chloro-5-(4-nitro)phenyl-5H-4-hydrazino-1,2,3-triazino-[4'.5':6,5]pyrano[3.2-h]quinoline (**234c**).

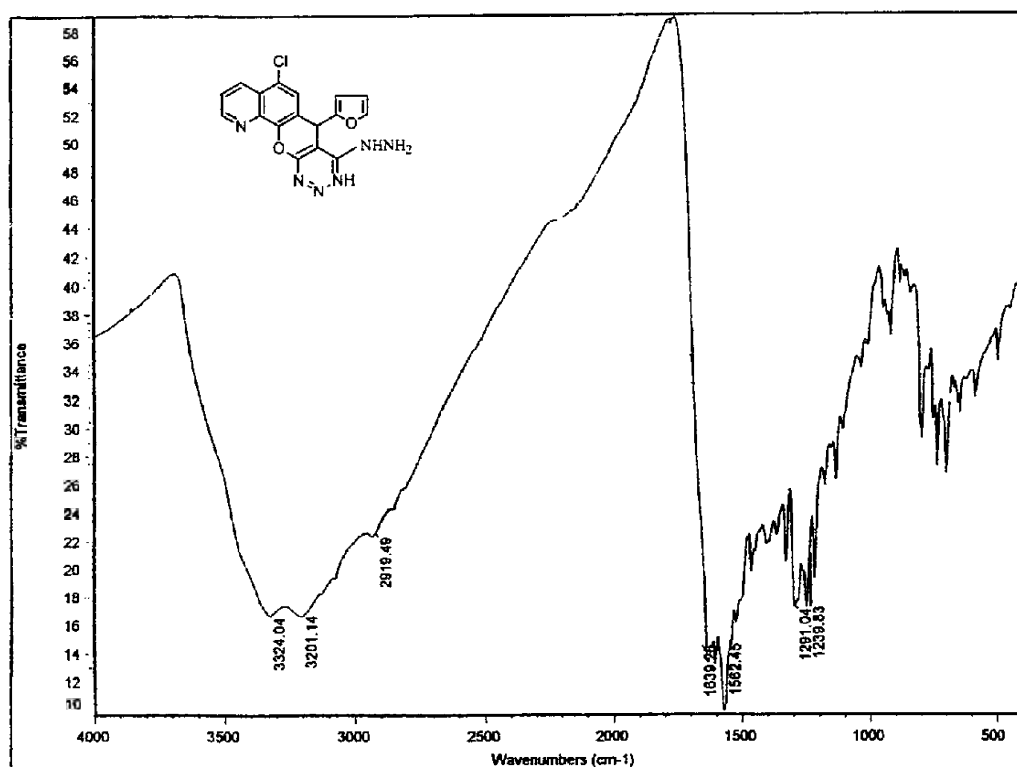


Fig.(75): 7-Chloro-5-furyl-5H-4-hydrazino-1,2,3-triazino[4',5':6,5]pyrano - [3,2-h]quinoline (234_d).

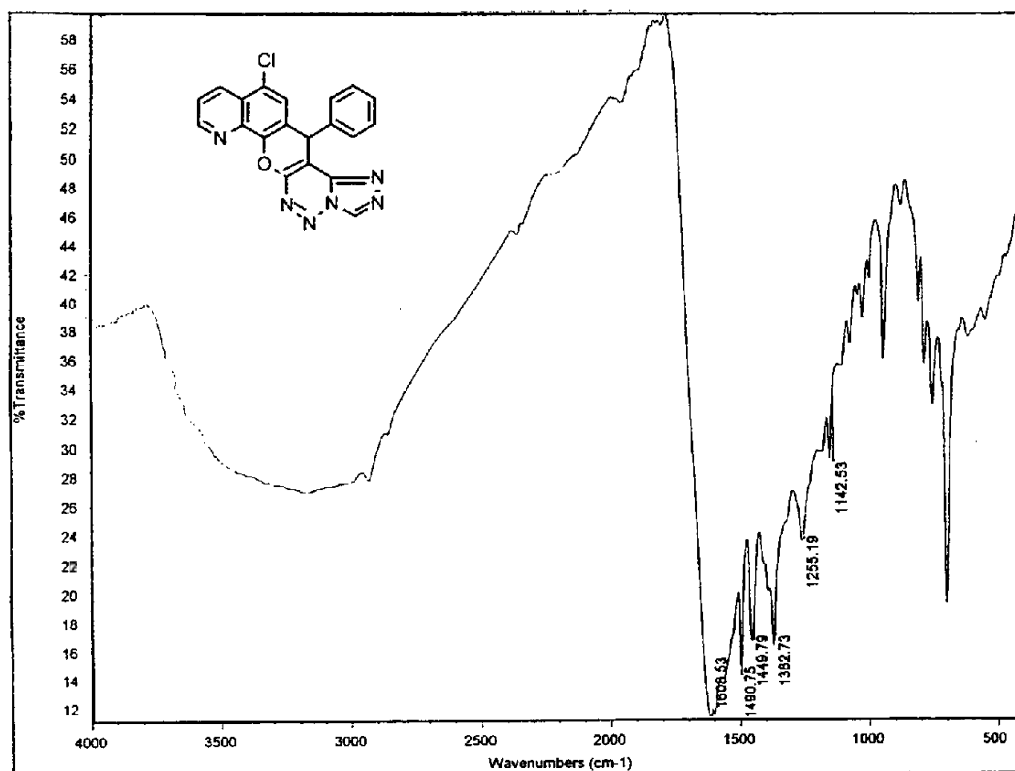
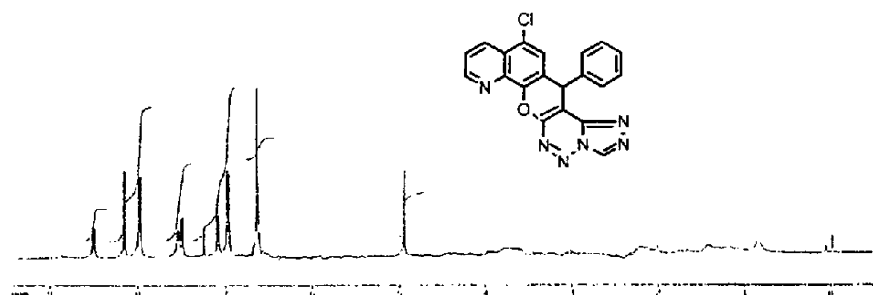


Fig.(76): 12-Chloro-14-phenyl-14H-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline (235_a).

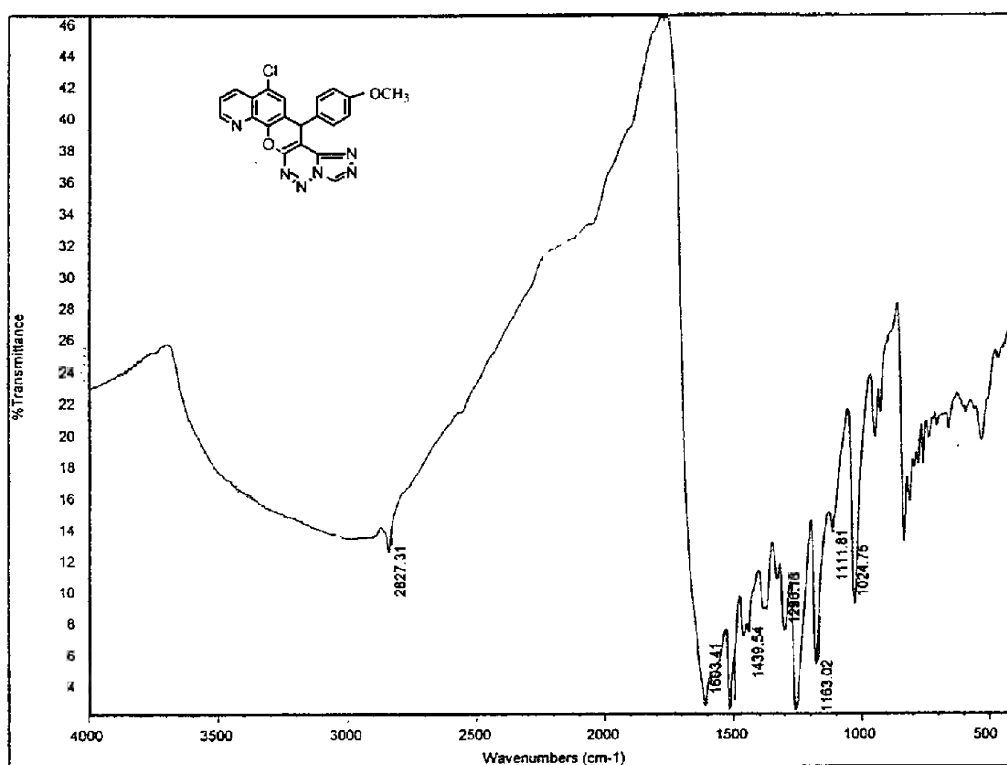


Fig.(77): 12-Chloro-14-(4-methoxy)phenyl-14H-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**235_b**).

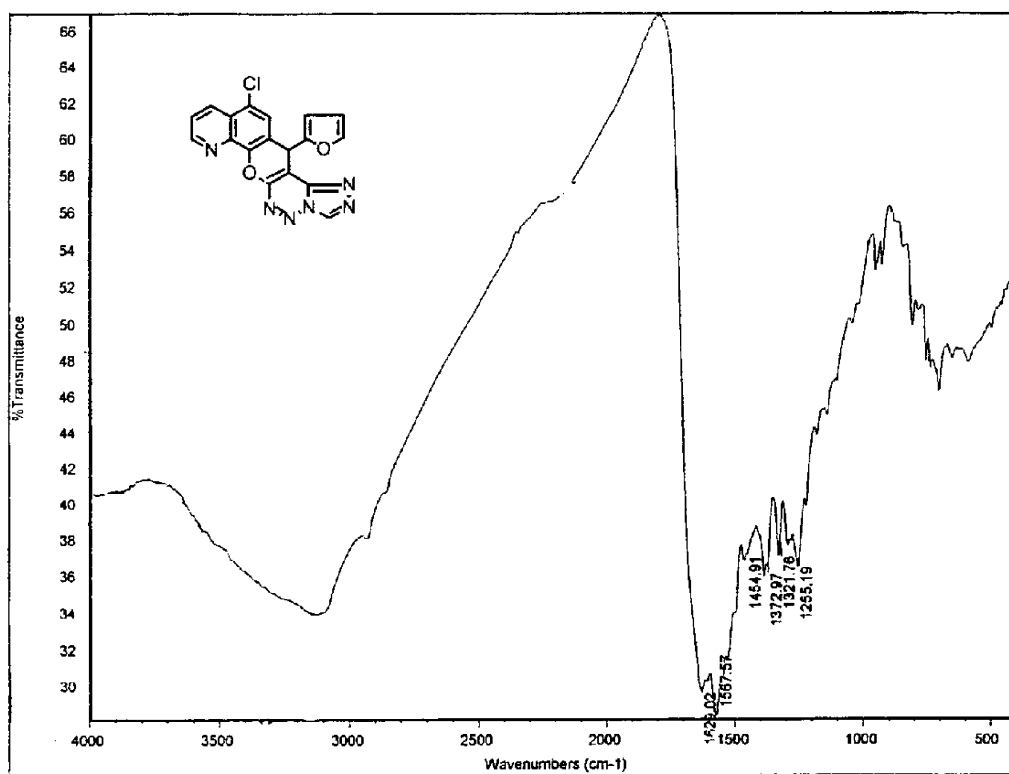


Fig.(78): 12-Chloro-14-furyl-14H-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline (**235_d**).

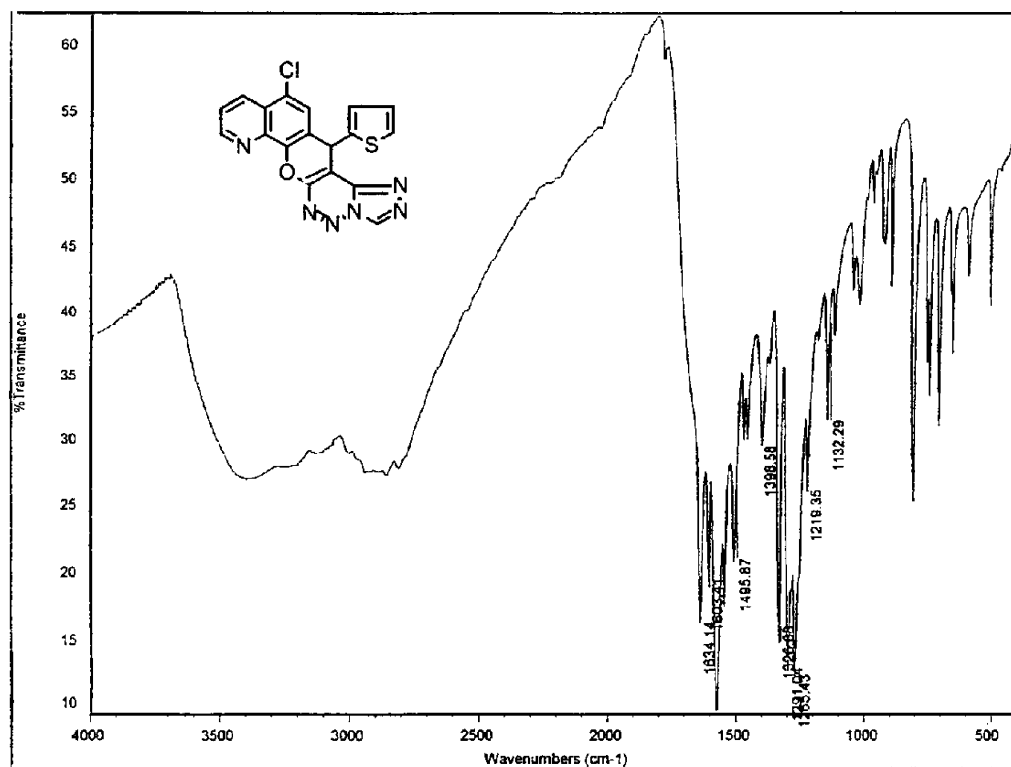


Fig.(79): 12-Chloro-14-thienyl-14H-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline (**235_c**).

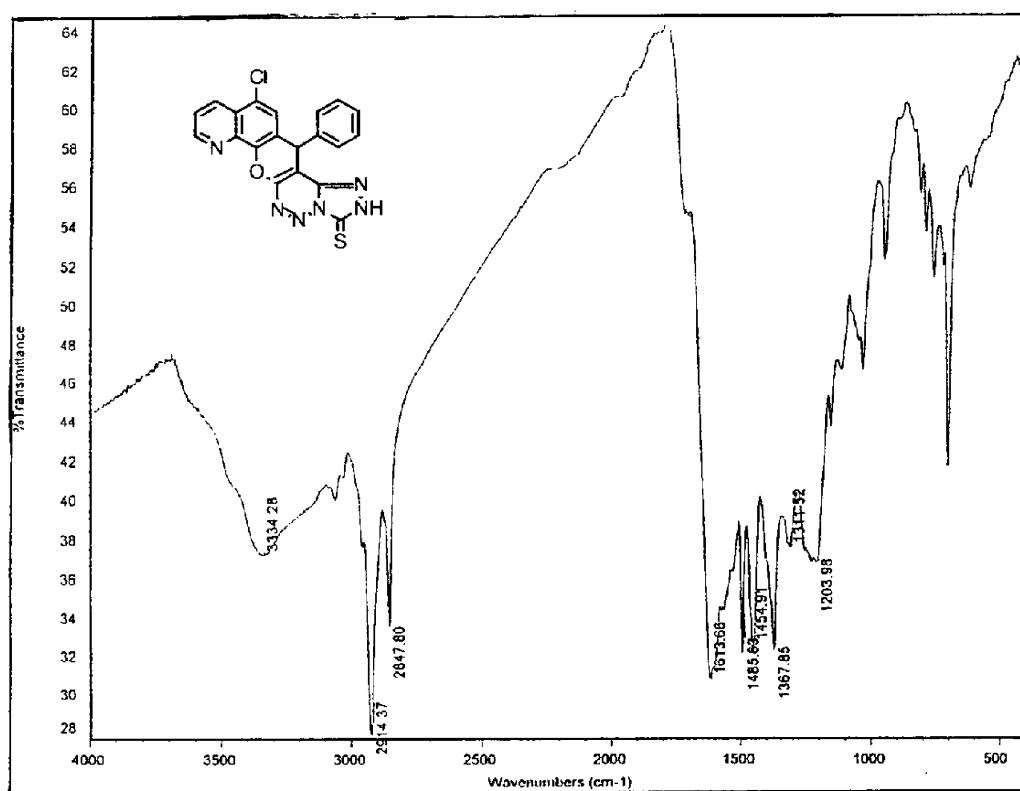
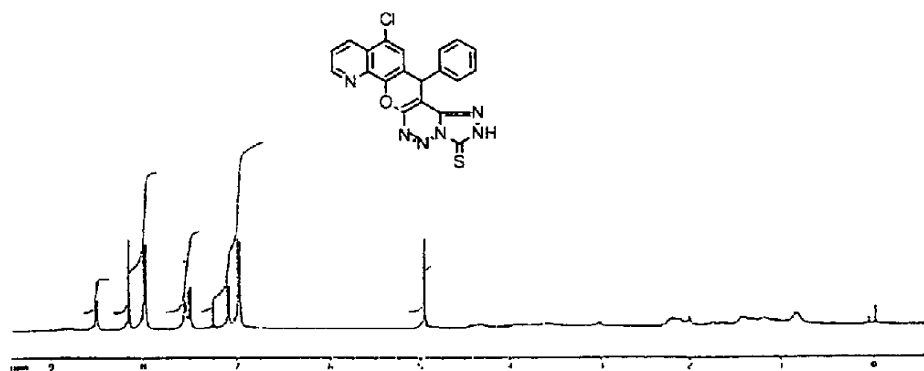


Fig.(80): 12-Chloro-14-phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3',4'']-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**236_a**).

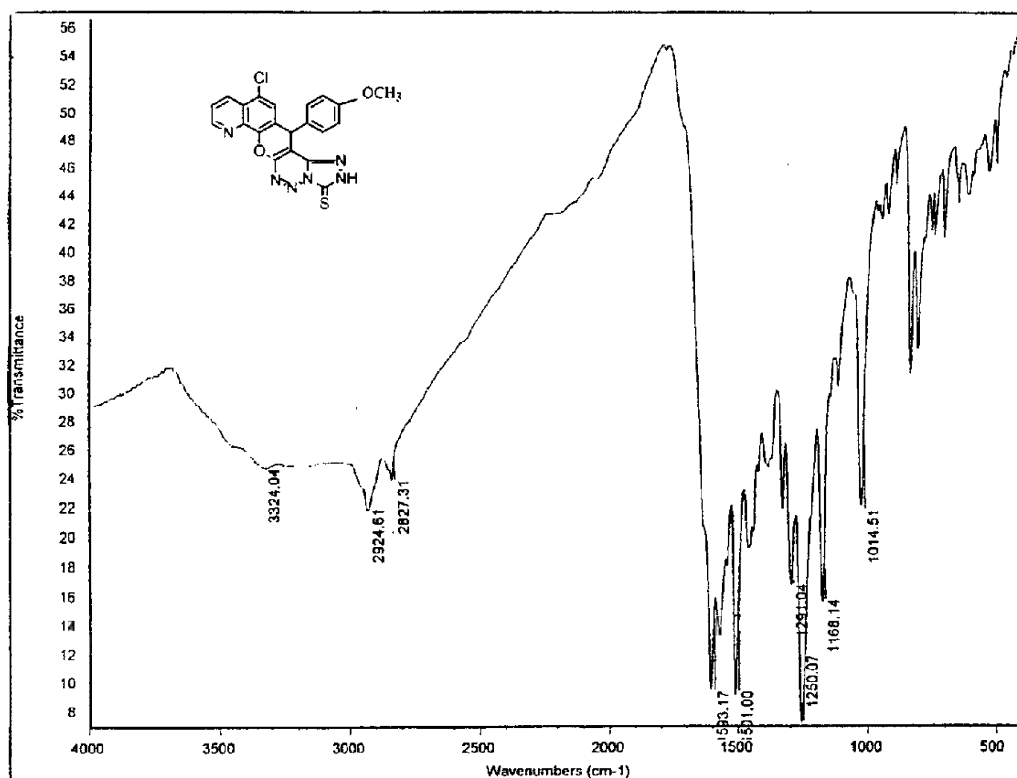


Fig.(81): 12-Chloro-14-(4-methoxy)phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo-[3'',4''-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**236_b**).

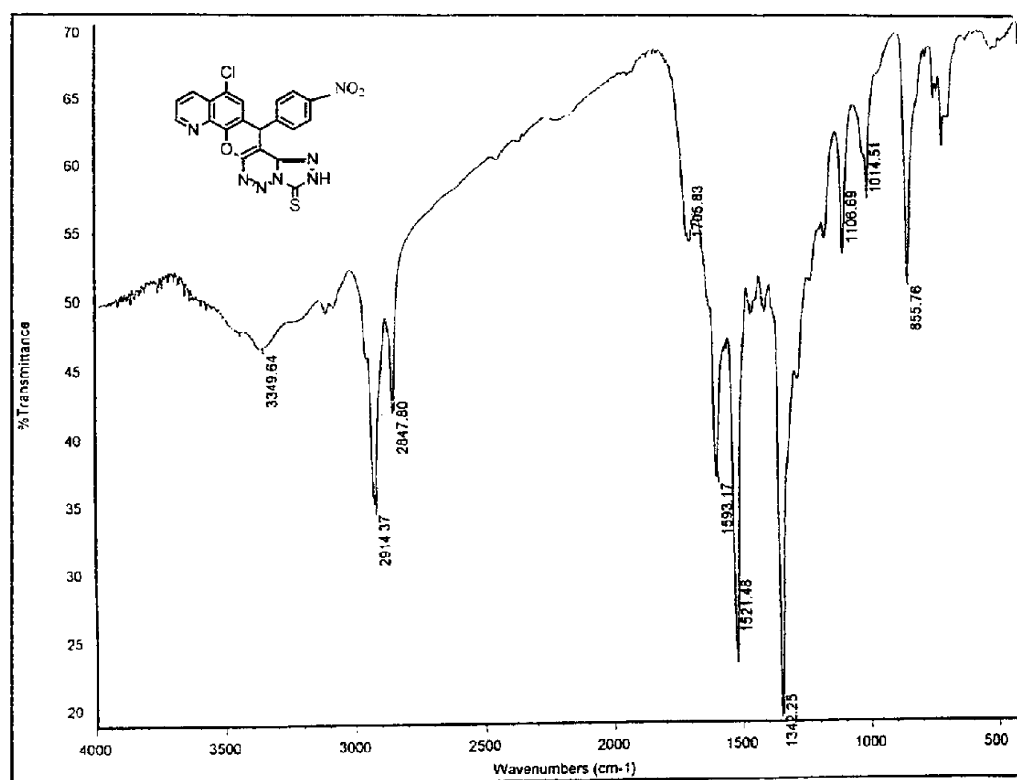


Fig.(82): 12-Chloro-14-(4-nitro)phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo-[3'',4''-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**236c**).

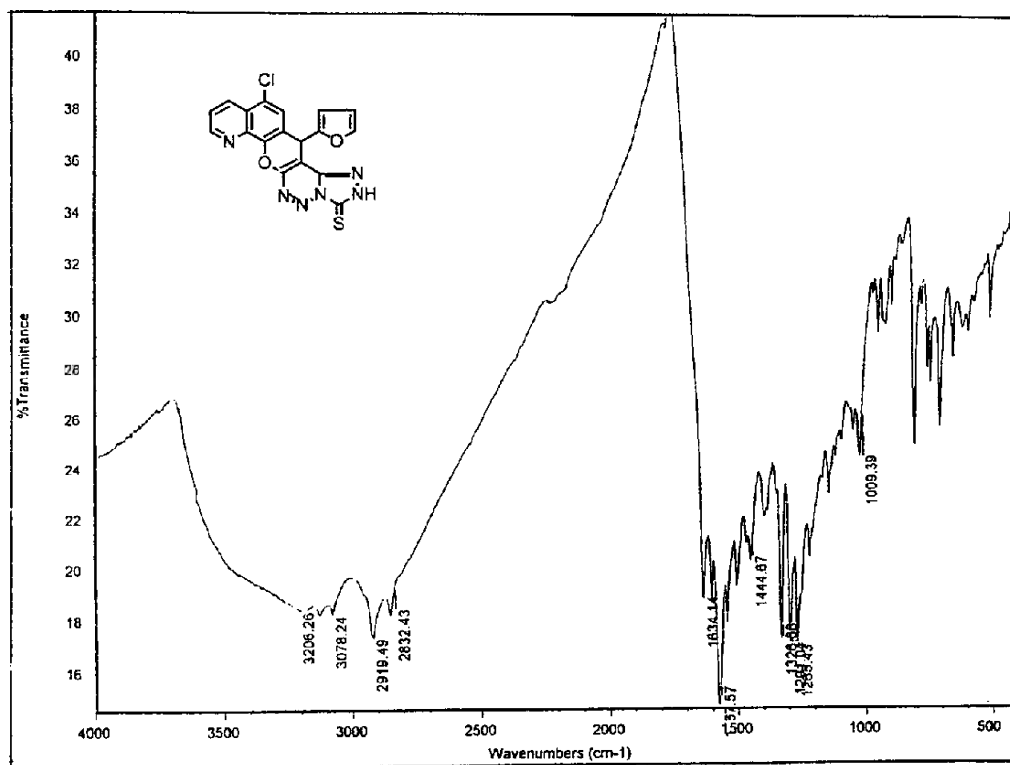


Fig.(83): 12-Chloro-14-furyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**236_d**).

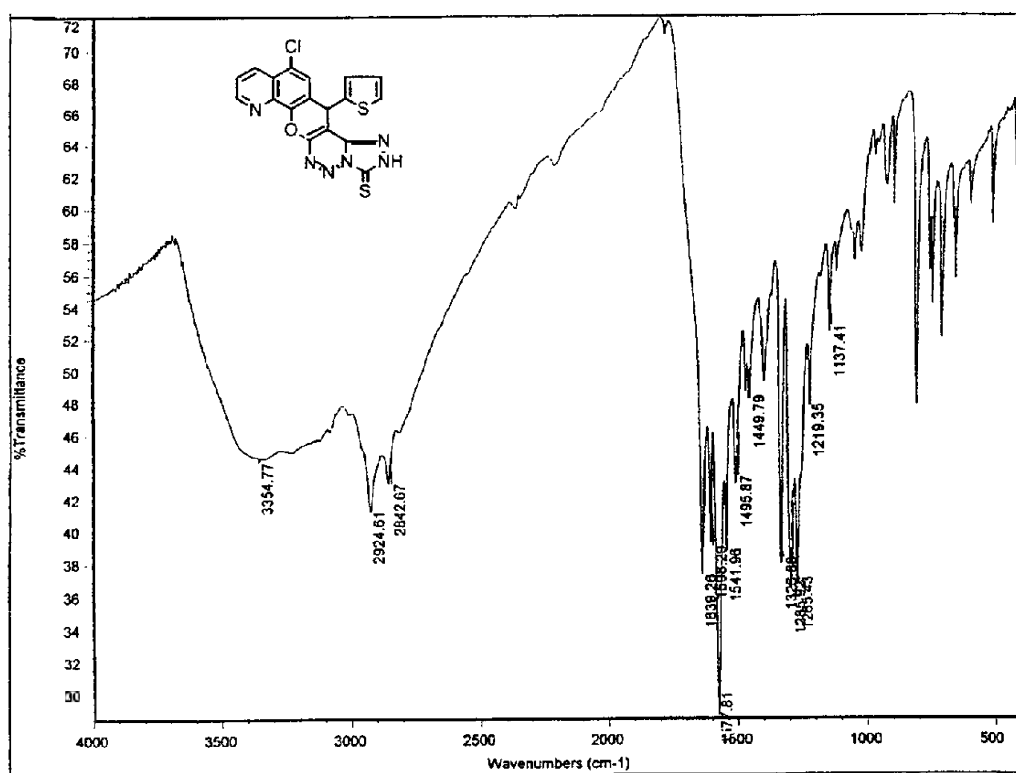


Fig.(84): 12-Chloro-14-thienyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3'',4''-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline (**236_c**).

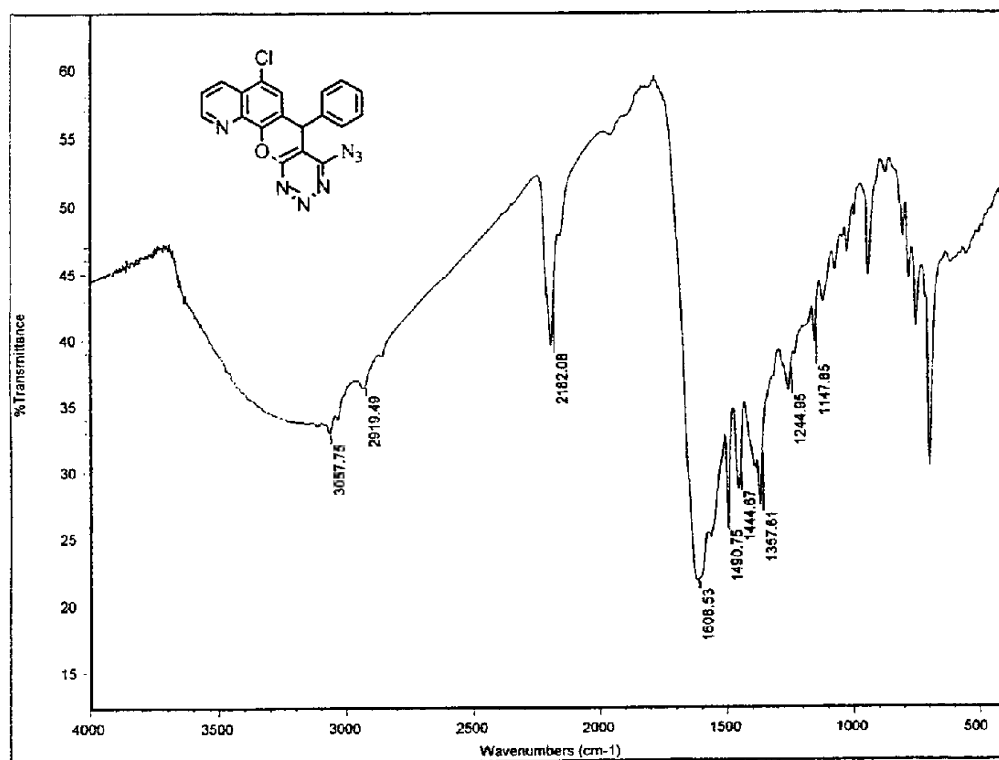


Fig.(85): 4-Azido-7-chloro-5-phenyl-5H-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]-quinoline (**237_a**).

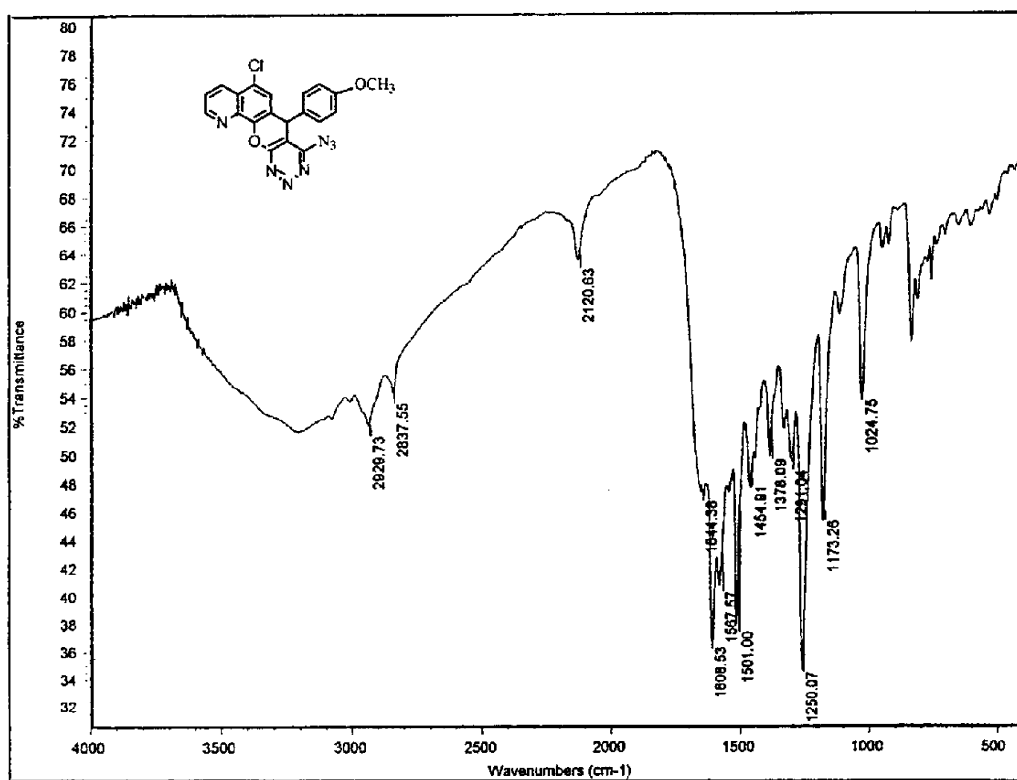


Fig.(86): 4-Azido-7-chloro-5-(4-methoxy)phenyl-5H-1,2,3-triazino[4',5':6,5]-pyrano[3,2-h]quinoline (**237_b**).

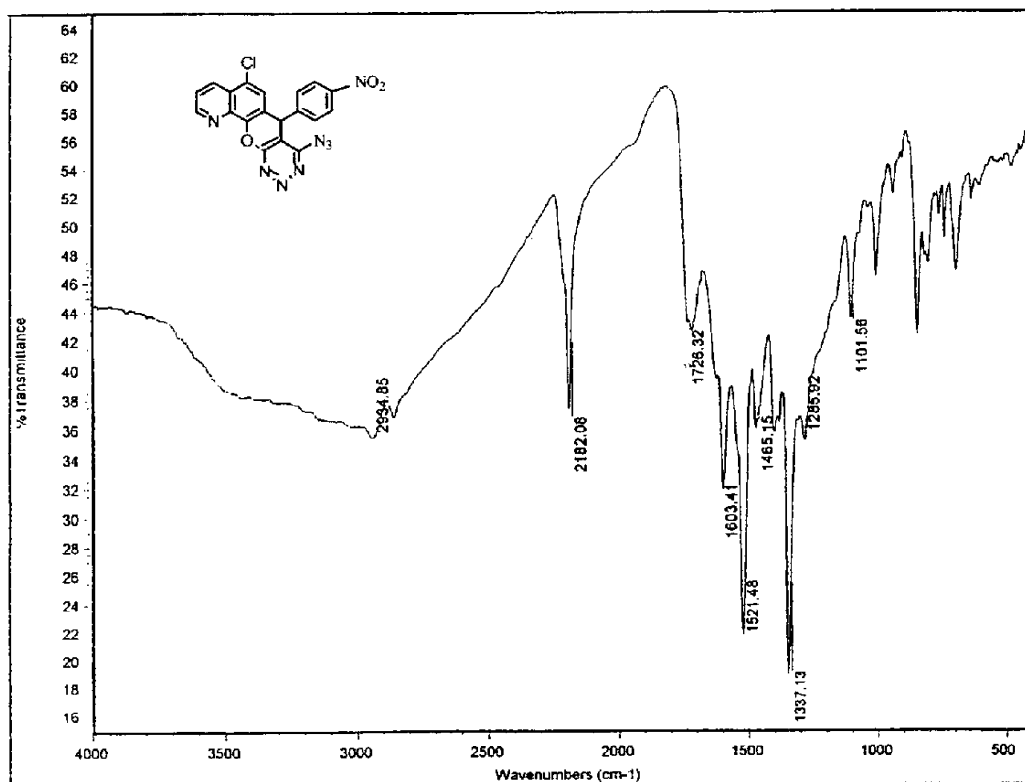


Fig.(87): 4-Azido-7-chloro-5-(4-nitro)phenyl-5H-1,2,3-triazino[4',5':6,5]-pyrano[3,2-h]quinoline (**237c**).

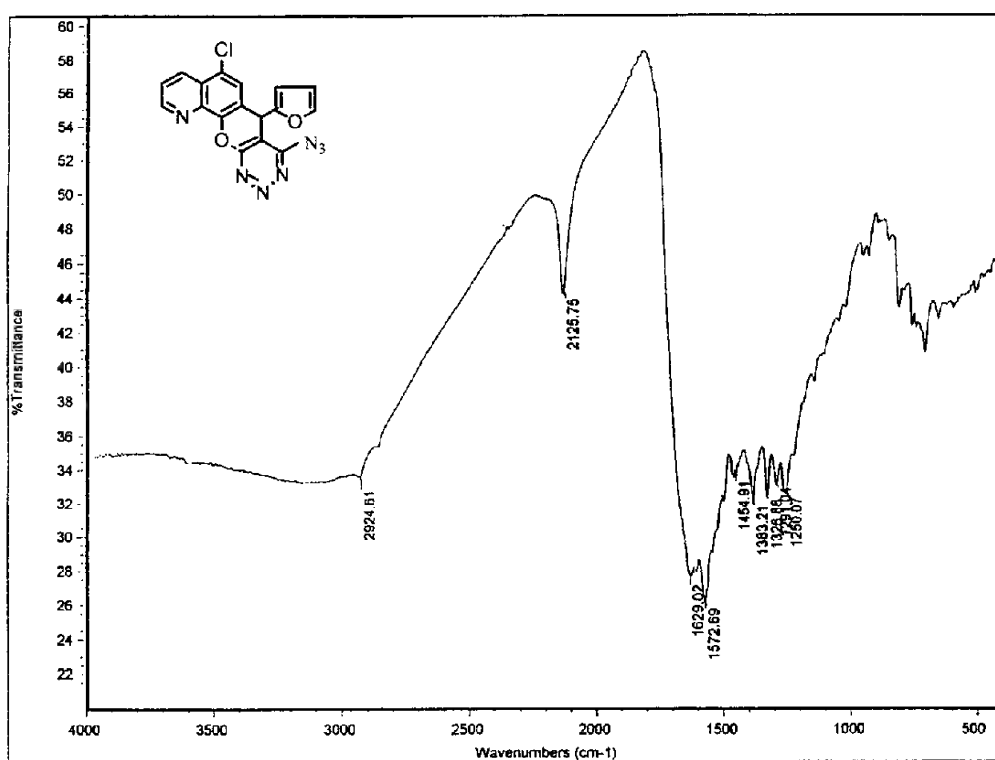


Fig.(88): 4-Azido-7-chloro-5-furyl-5H-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline (237_d).

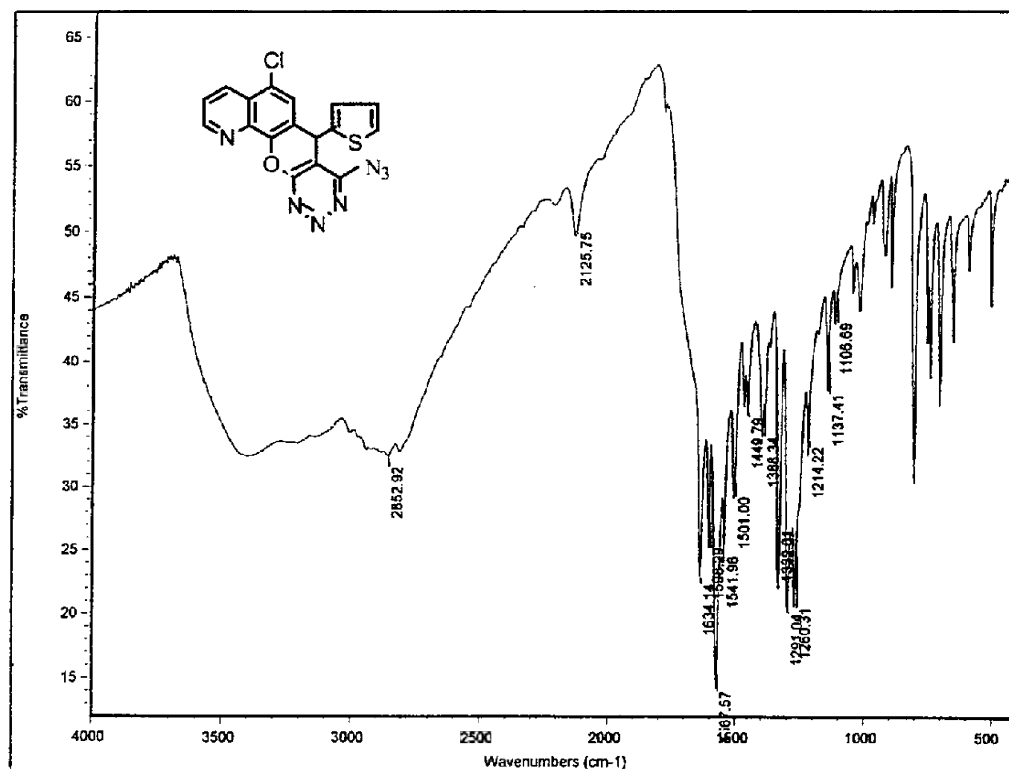


Fig.(89): 4-Azido-7-chloro-5-thienyl-5H-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline (**237_e**).

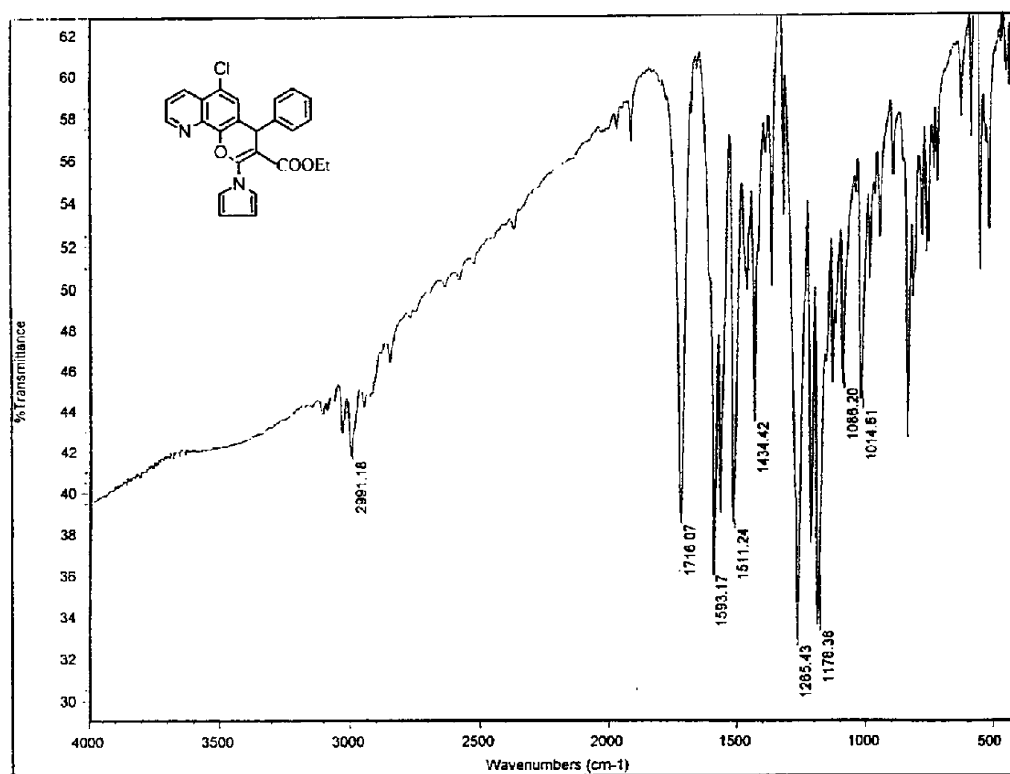


Fig.(90): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**238_a**).

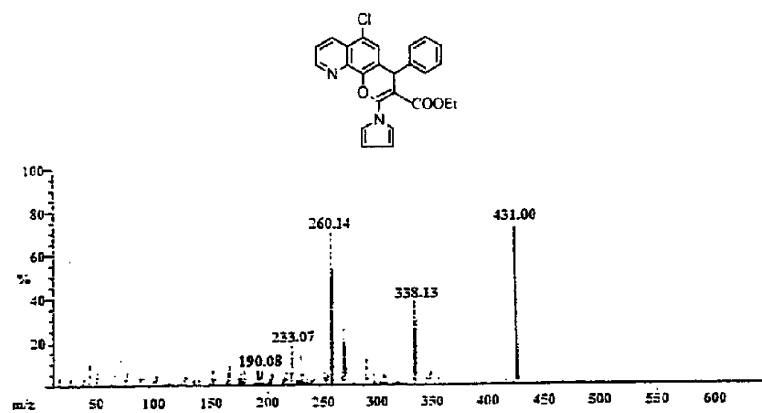


Fig.(91): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**238_a**).

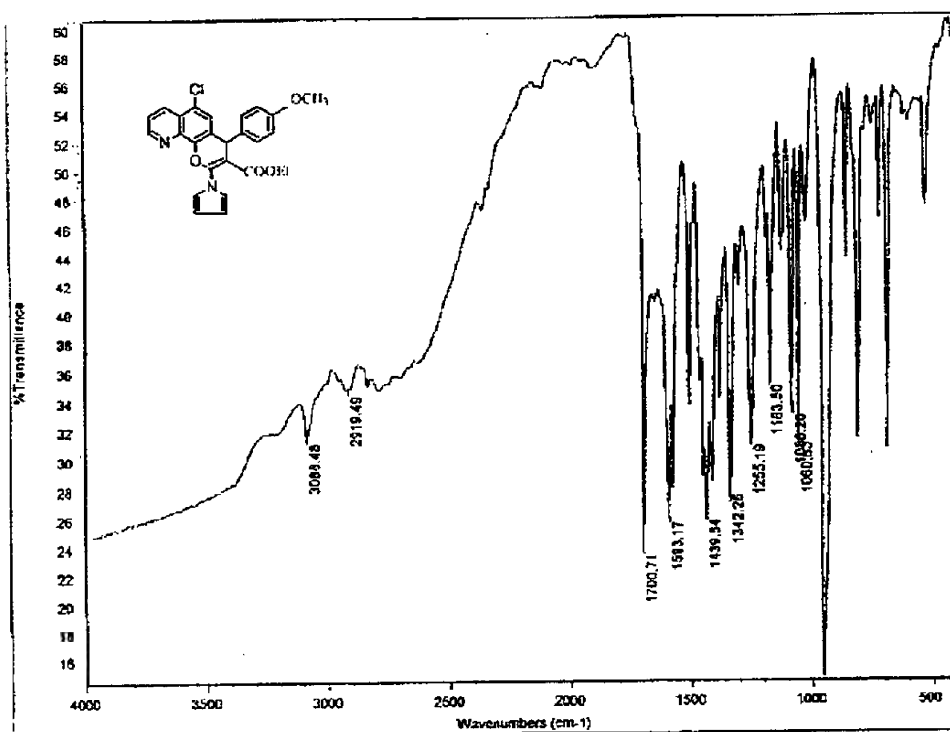


Fig.(92): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate (**238_b**).

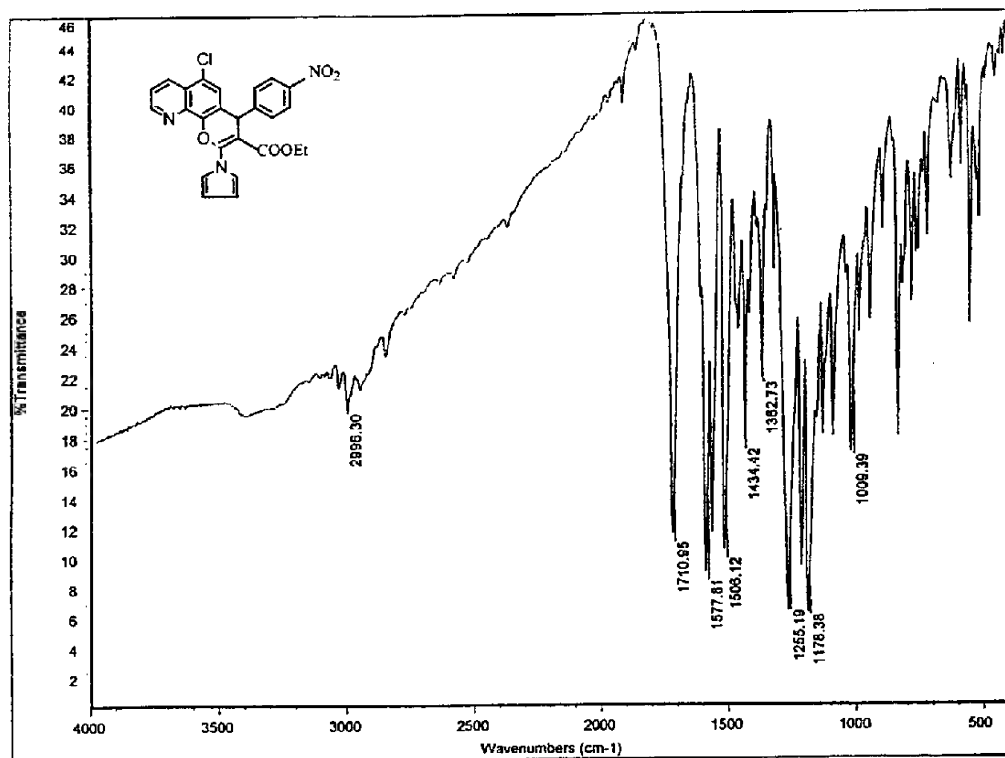


Fig.(93): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano[3,2-h]-quinoline-3-carboxylate (**238_c**).

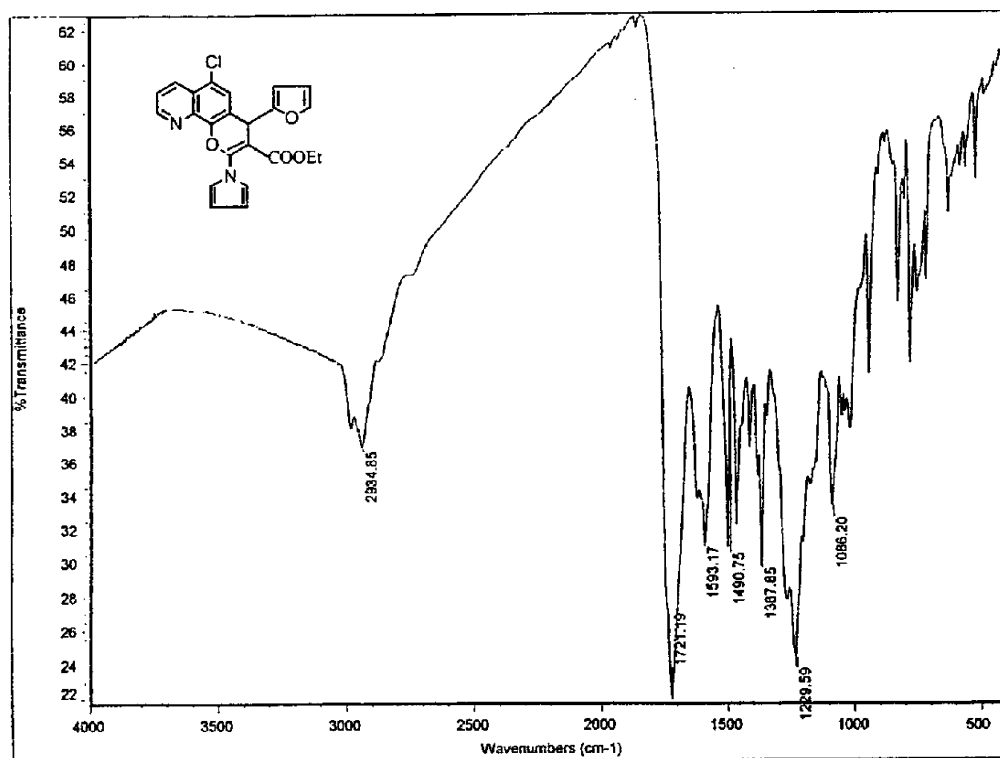


Fig.(94): Ethyl 2-(1-pyrrolyl)-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**238_d**).

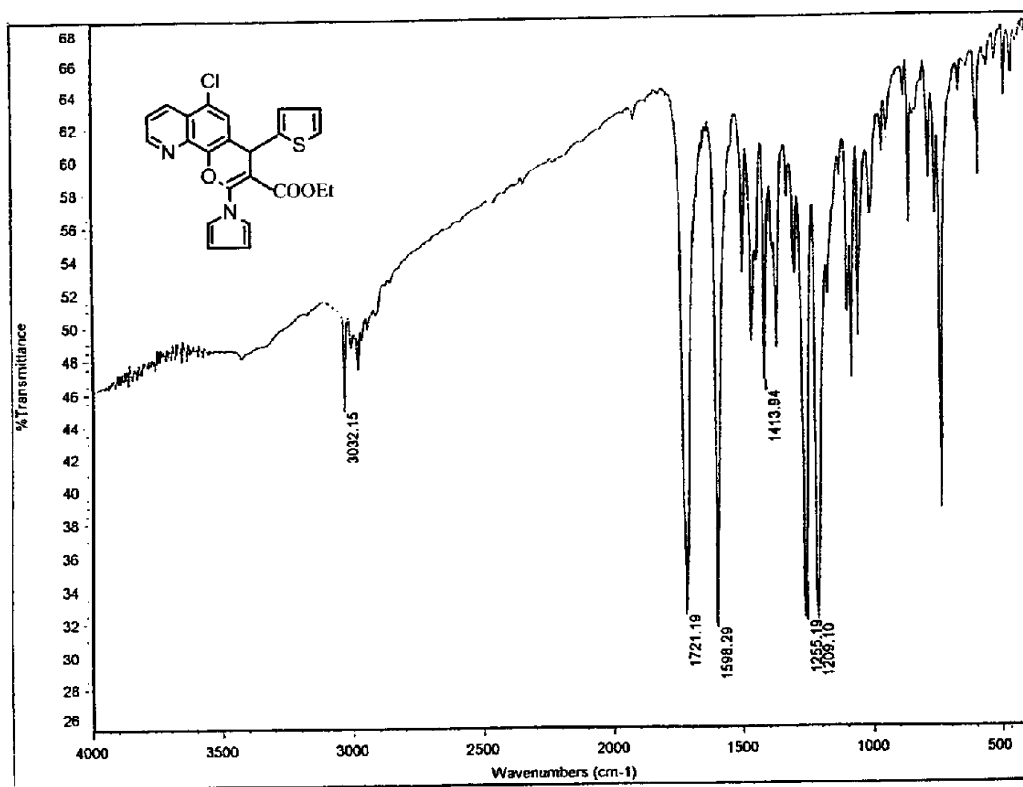


Fig.(95): Ethyl 2-(1-pyrrolyl)-6-chloro-4-thienyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**238_c**).

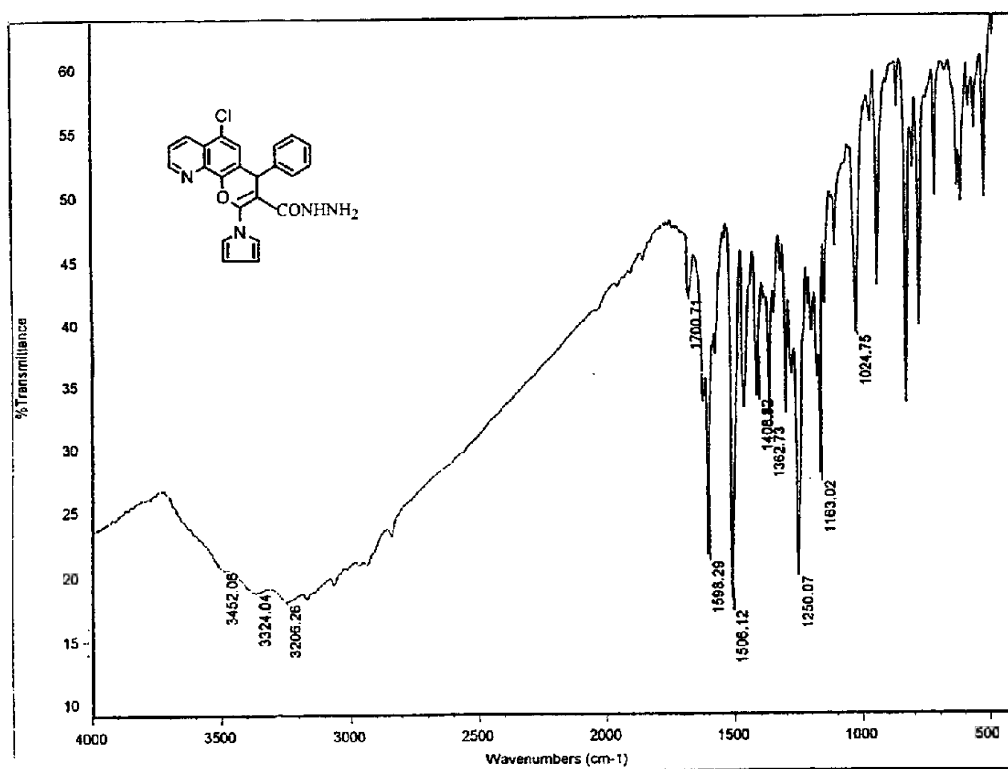


Fig.(96): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbohydrazide (**239_a**).

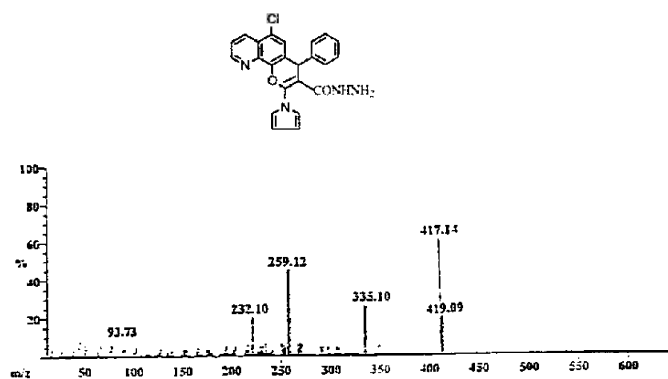
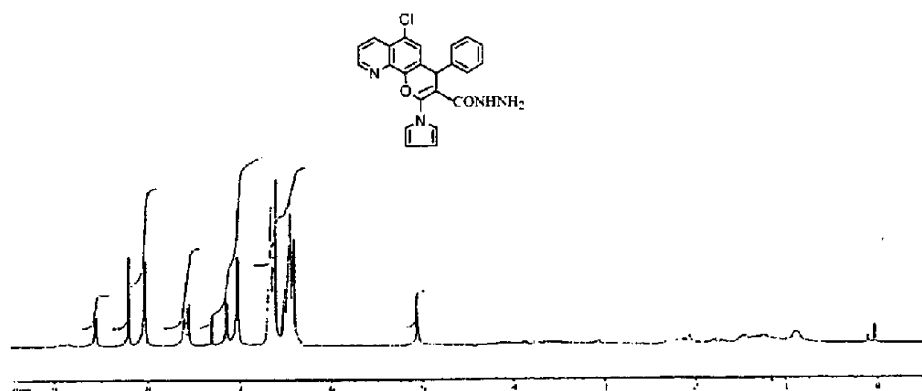


Fig.(97): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbohydrazide (**239_a**).

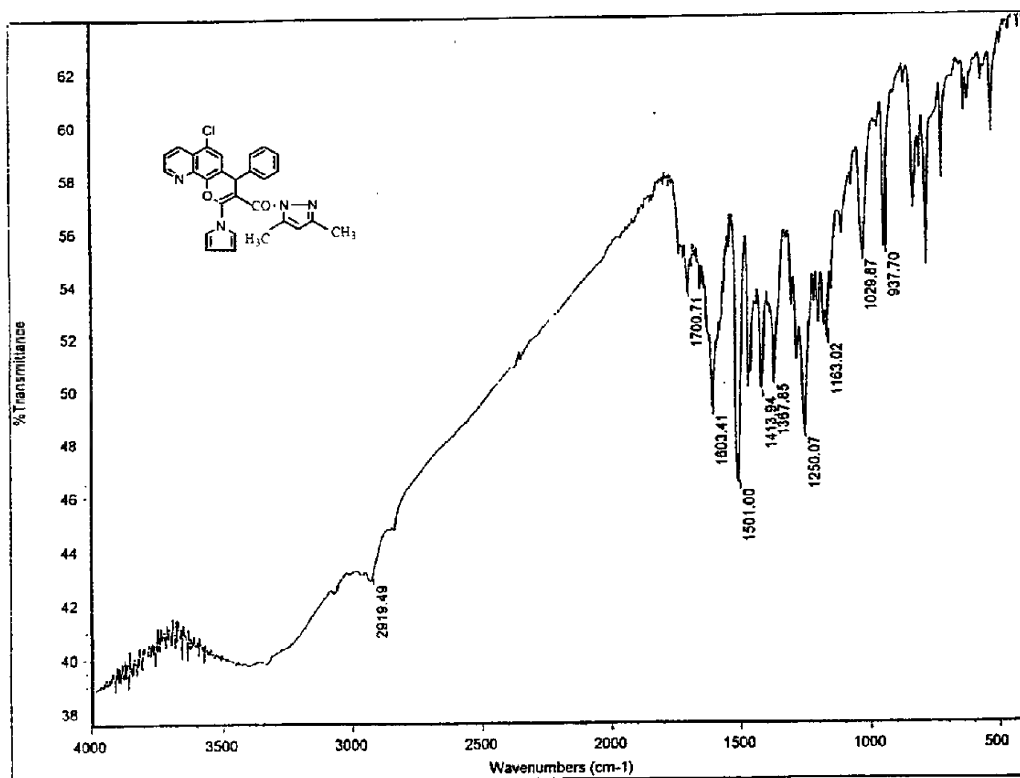


Fig.(98): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-phenyl-4H-pyrano[3,2-h]quinoline (**240_a**).

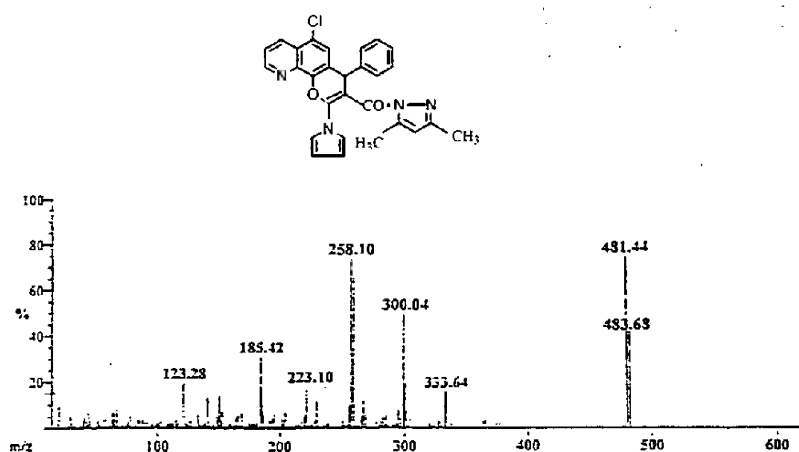
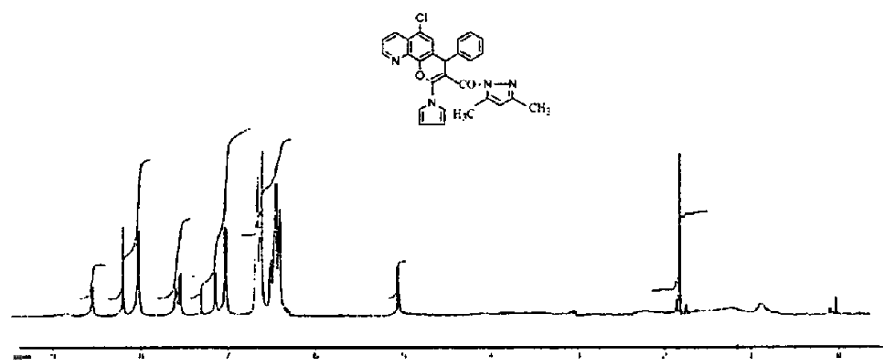


Fig.(99): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-phenyl-4H-pyrano[3,2-h]quinoline (**240_a**).

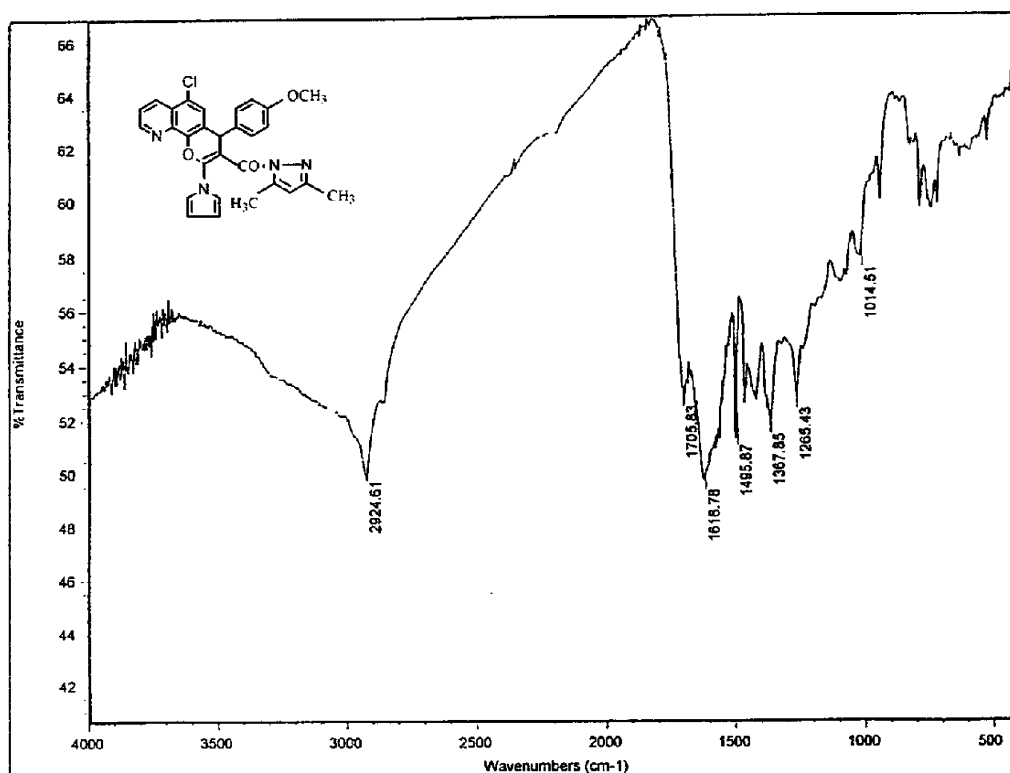


Fig.(100): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-(4-methoxy)phenyl-4H-pyrano[3,2-h]quinoline (**240_b**).

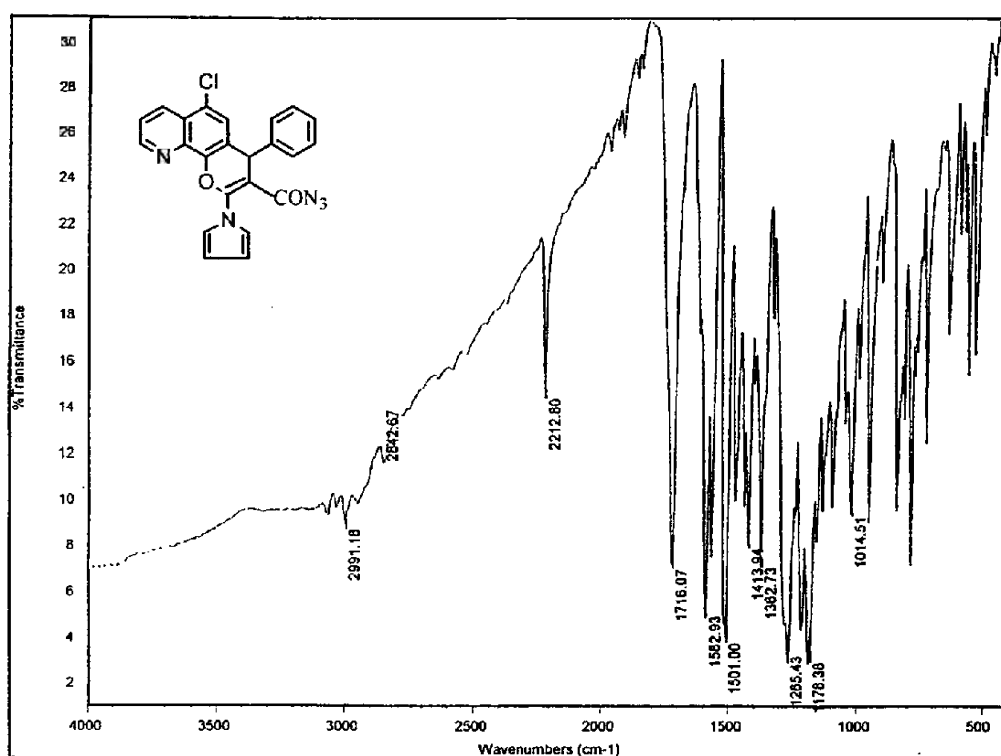
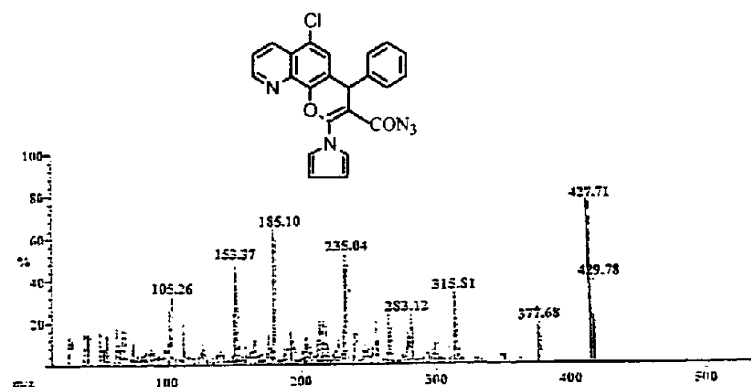


Fig.(101): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinolin-3-oylazine (**241_a**).

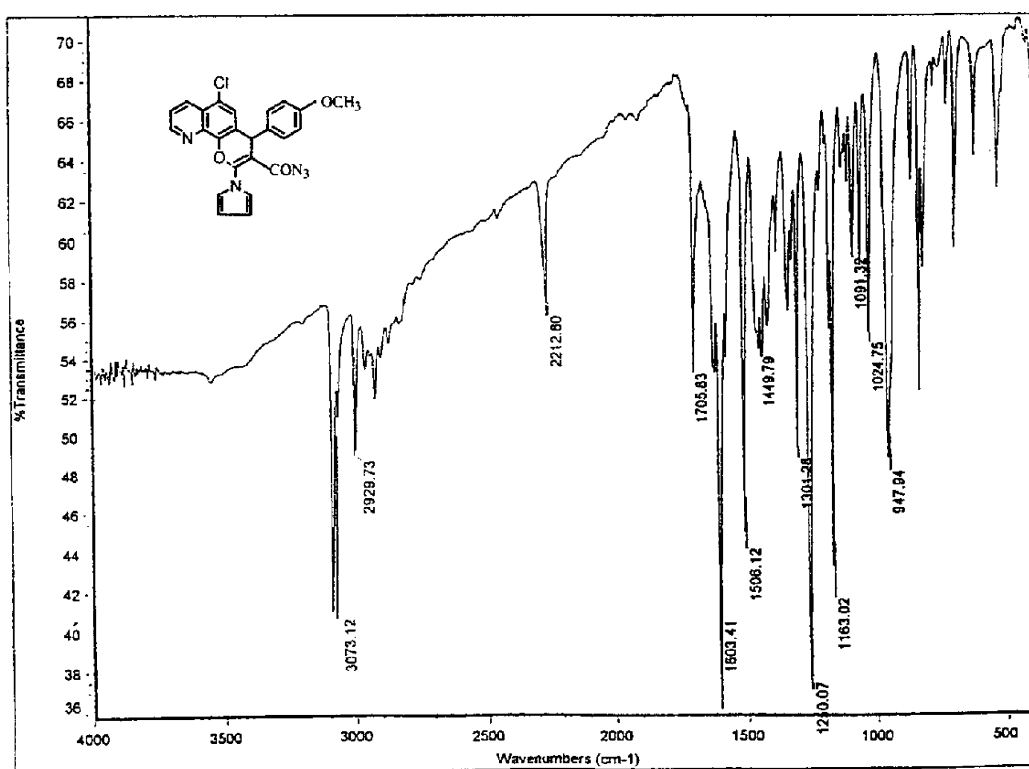


Fig.(102): 6-Chloro-2-(1-pyrrolyl)-4-(4-methoxyphenyl)-4H-pyrano[3,2-h]-quinolin-3-ylazide (**241b**).

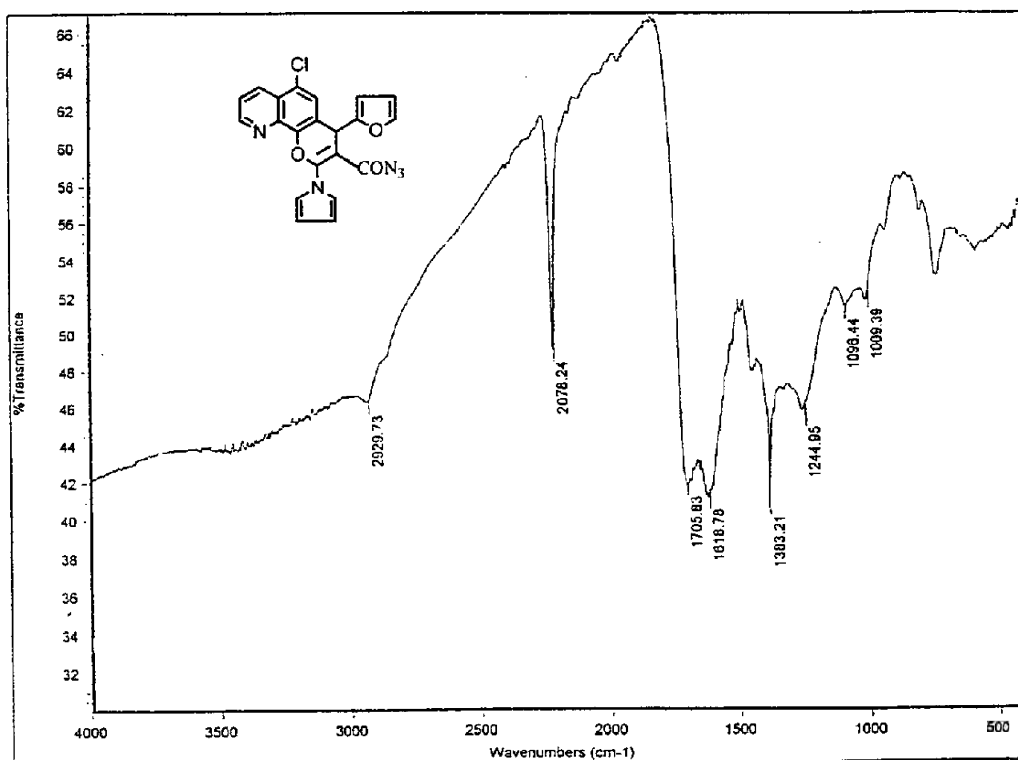


Fig.(103): 6-Chloro-2-(1-pyrrolyl)-4-furyl-4H-pyrano[3,2-h]quinolin-3-oylazide (**241d**).

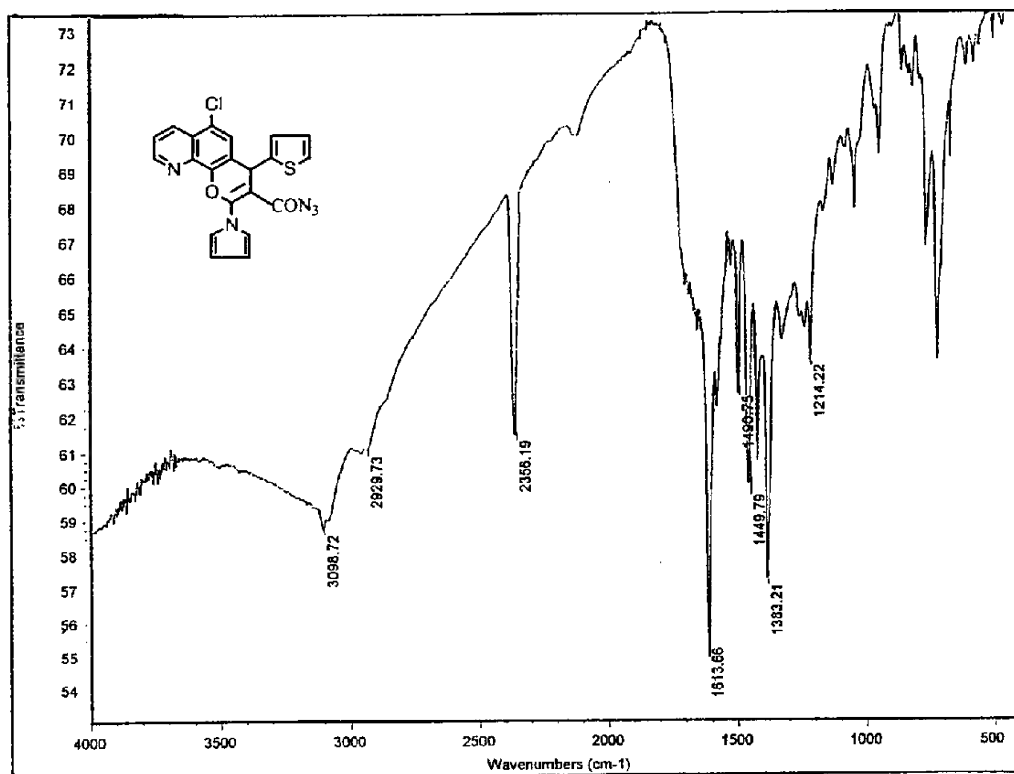


Fig.(104): 6-Chloro-2-(1-pyrrolyl)-4-thienyl-4H-pyrano[3,2-h]quinolin-3-oylazine (**241c**).

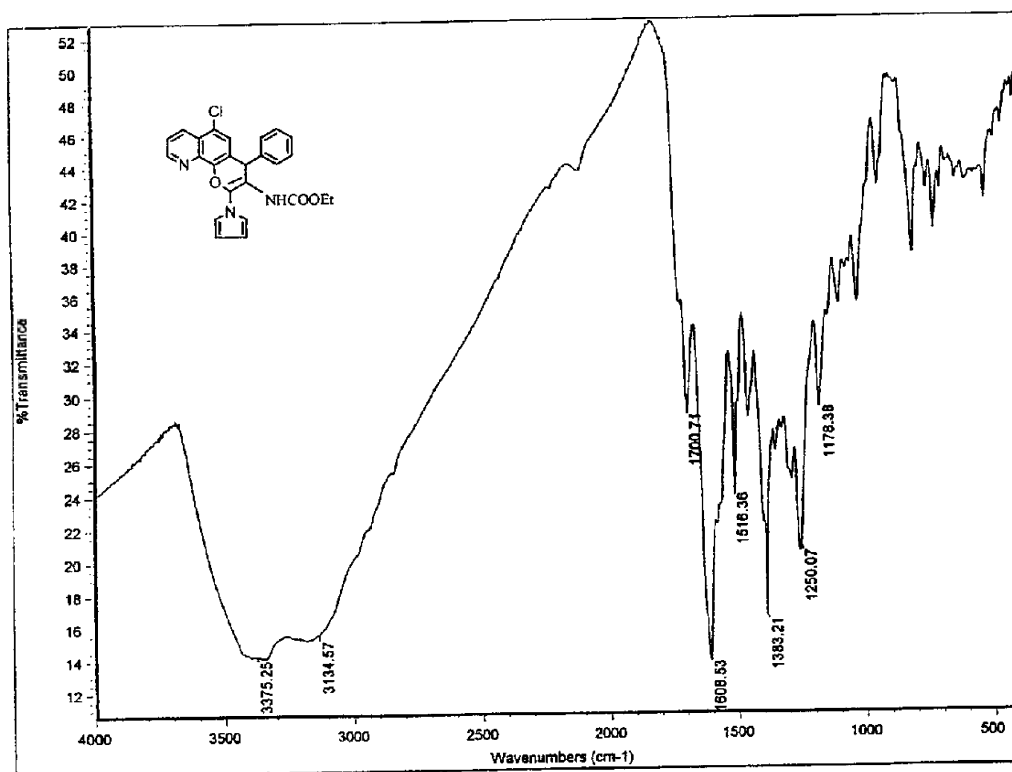


Fig.(105): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbamate (**242_a**).

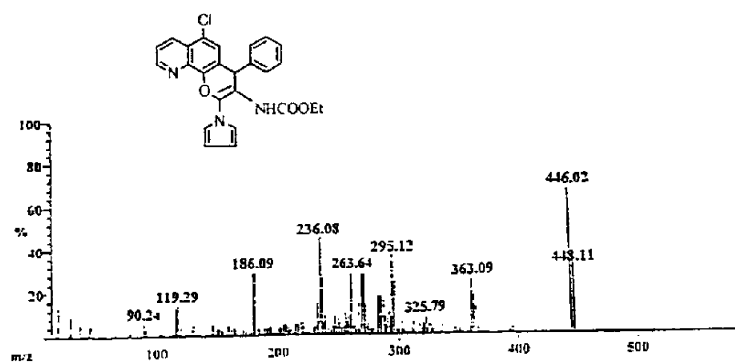
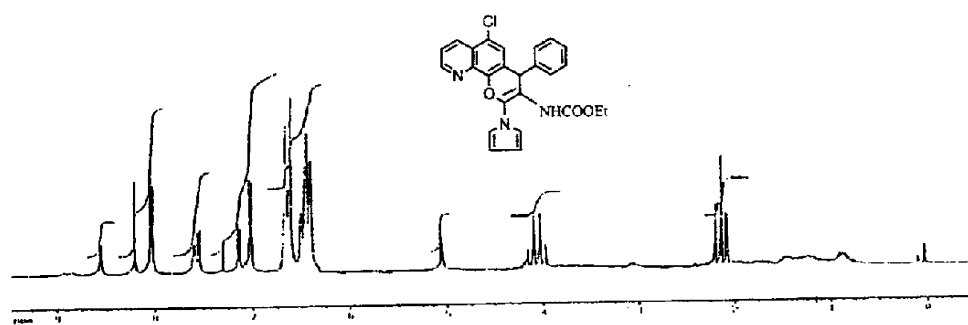


Fig.(106): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbamate (**242_a**).

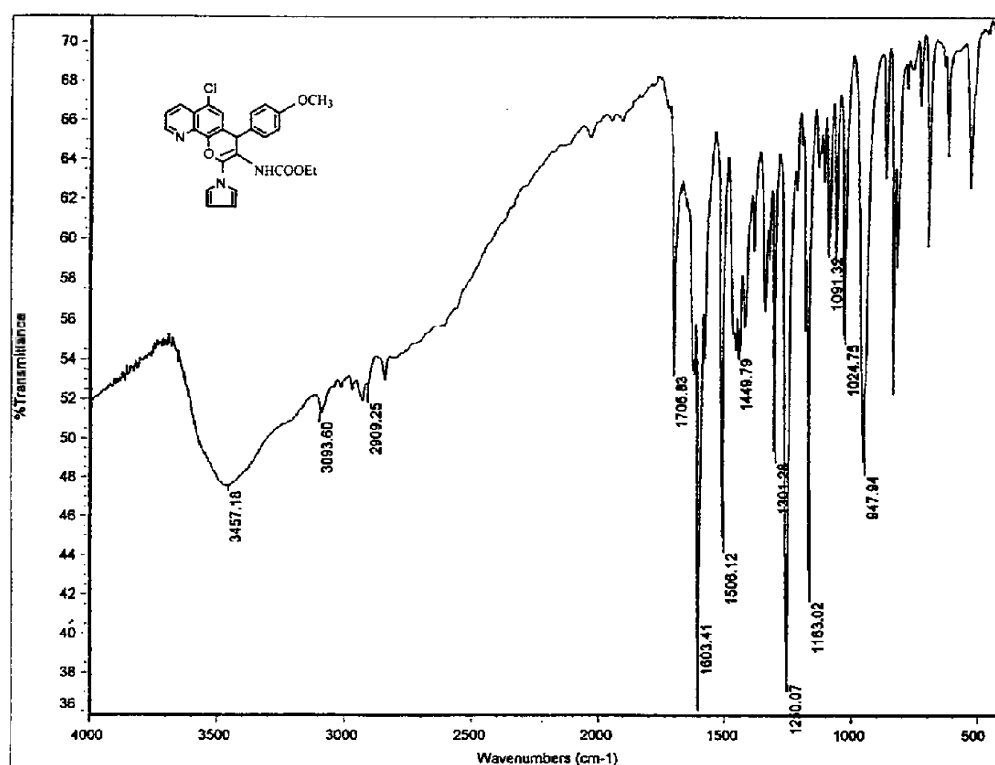


Fig.(107): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carbamate (**242_b**).

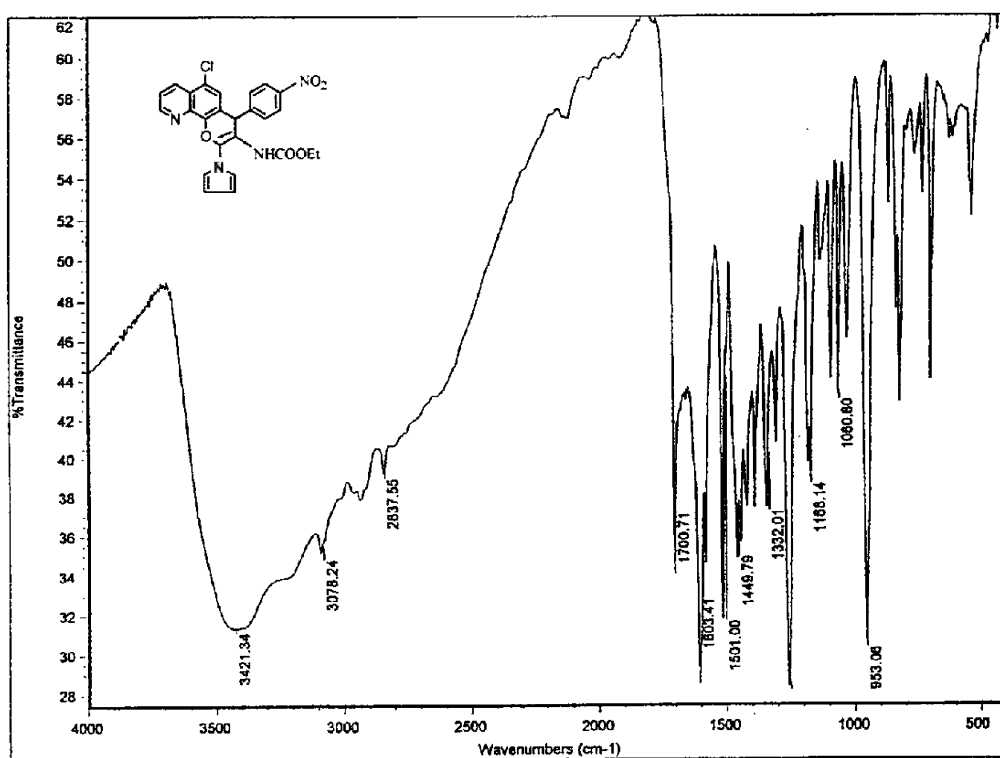


Fig.(108): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline-3-carbamate (**242c**).

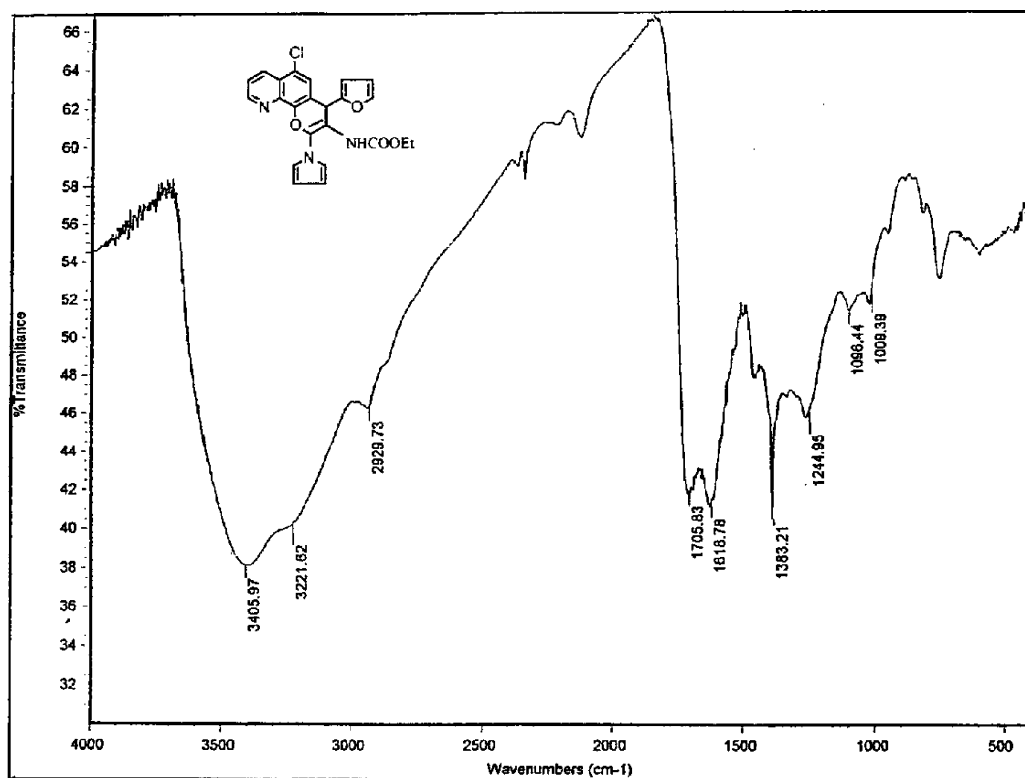


Fig.(109): Ethyl 2-(1-pyrrolyl)-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carbamate (**242_d**).

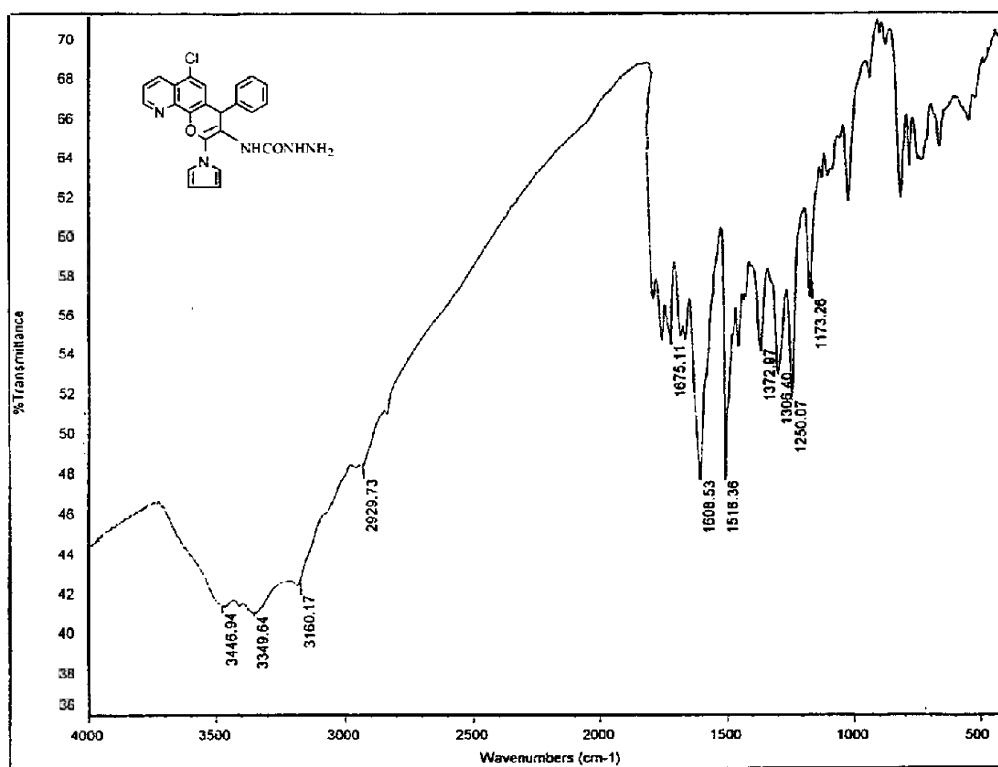
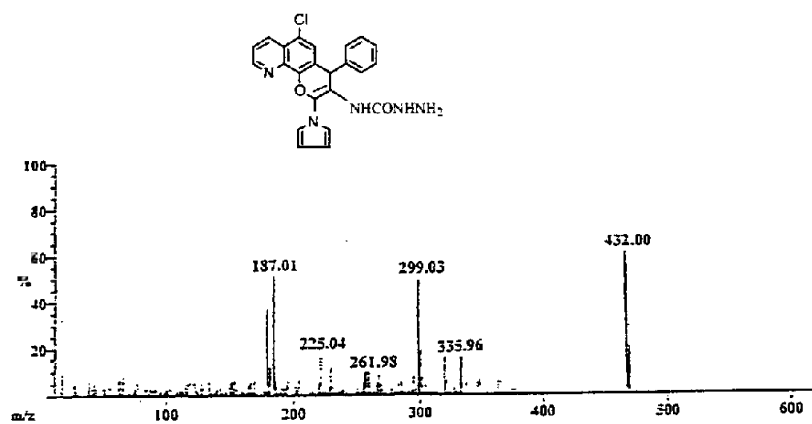


Fig.(110): 4-[2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinolin-3-yl]-semicarbazide (**243_a**).

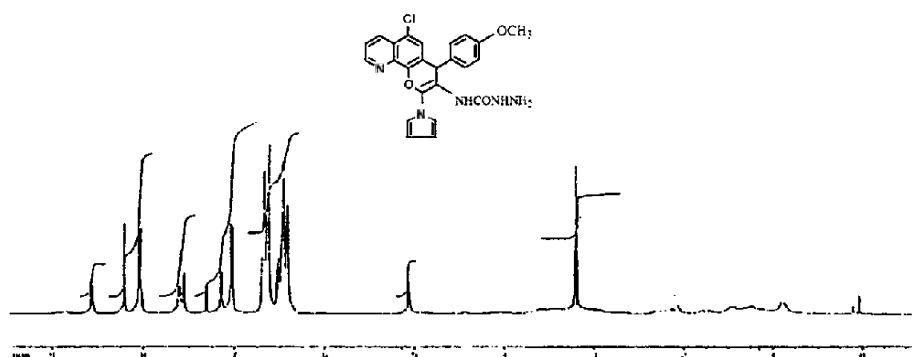


Fig.(111): 4-[2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl]-4H-pyrano-[3,2-h]quinolin-3-yl]semicarbazide (**243_b**).

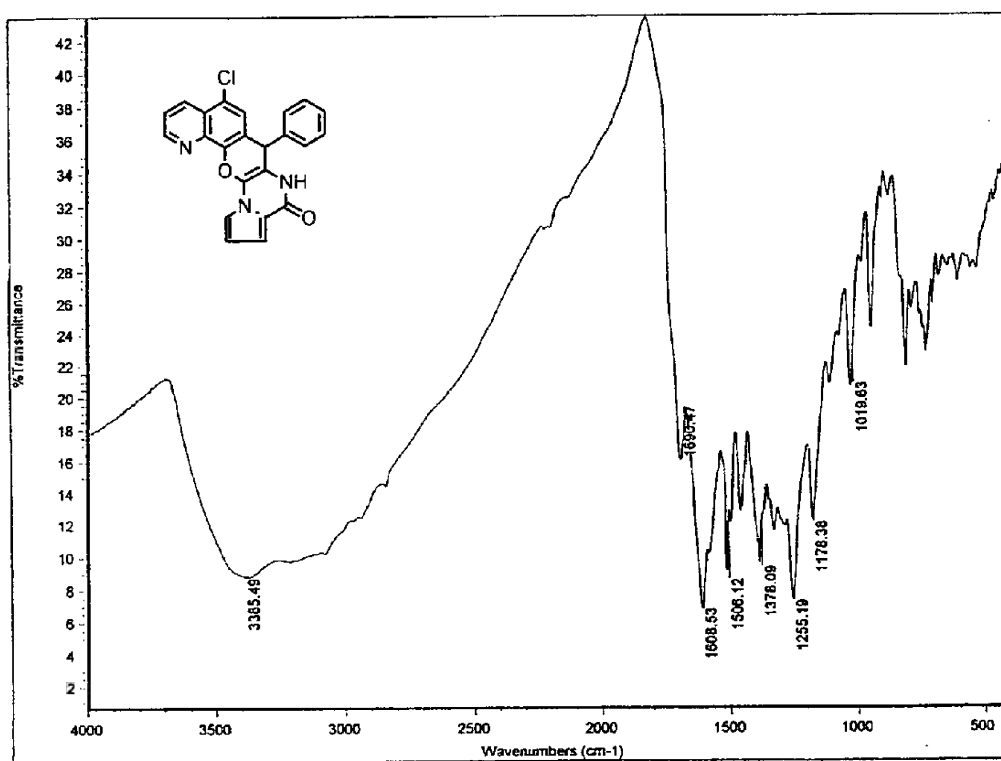
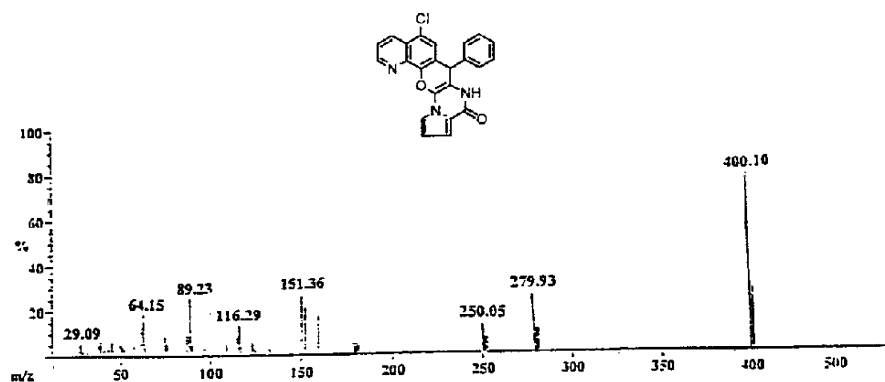


Fig.(112): 5-Chloro-7-phenyl-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**244_a**).

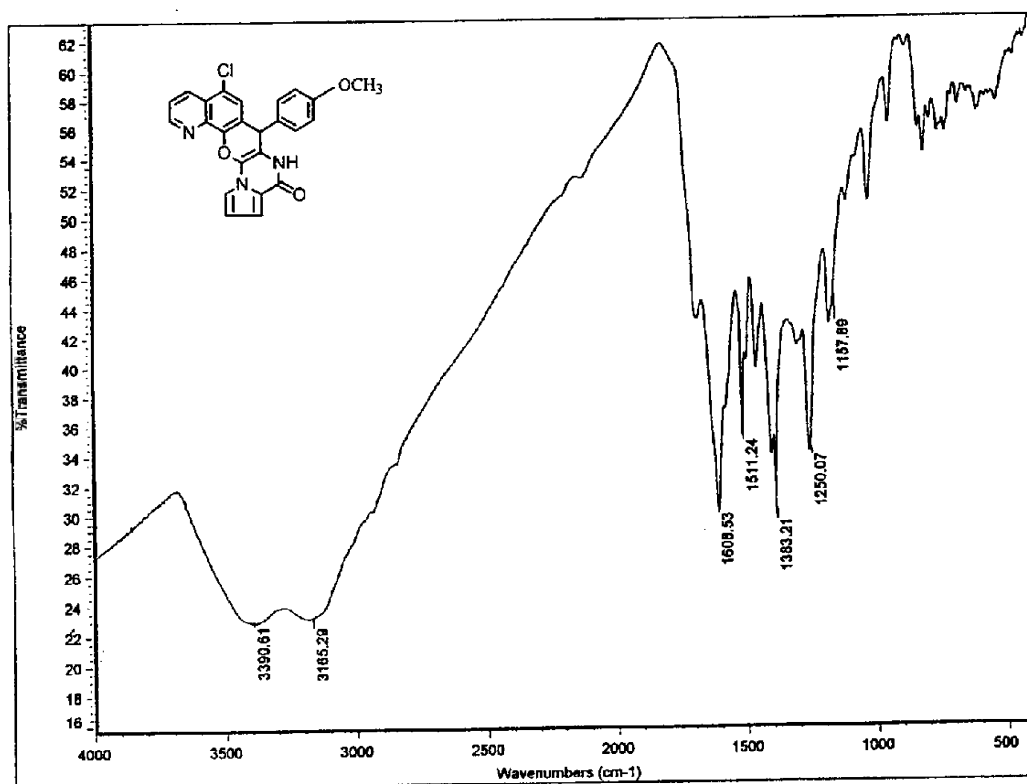


Fig.(113): 5-Chloro-7-(4-methoxy)phenyl-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**244_b**).

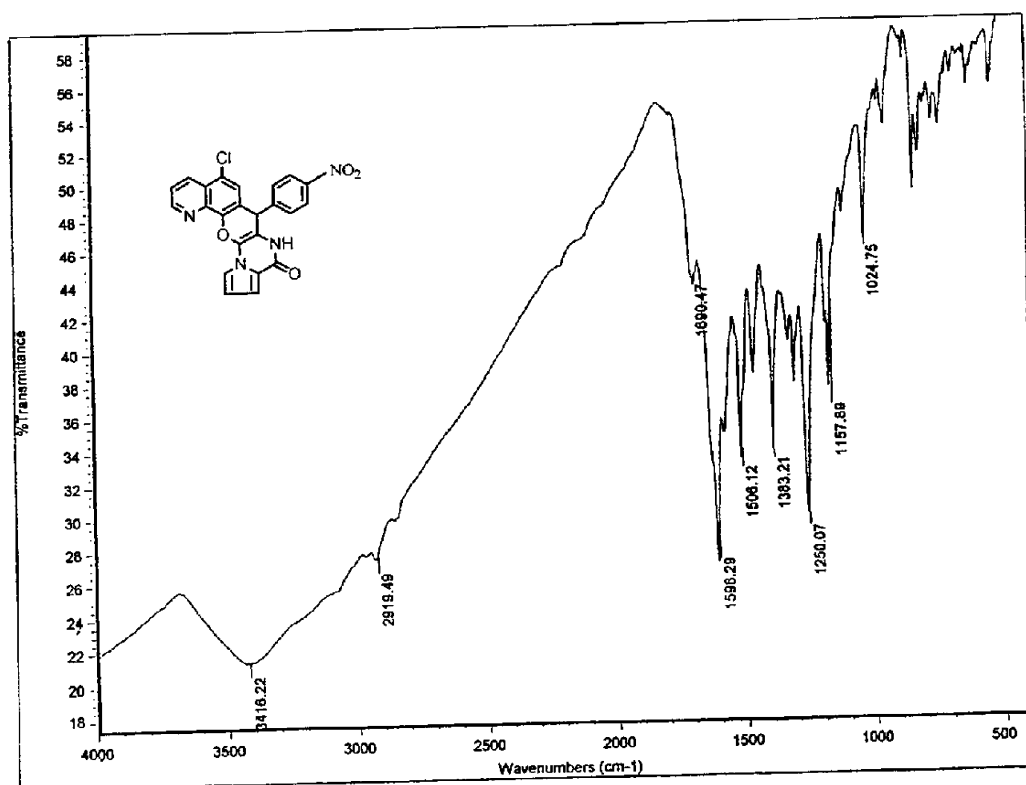


Fig.(114): 5-Chloro-7-(4-nitro)phenyl-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**244_c**).

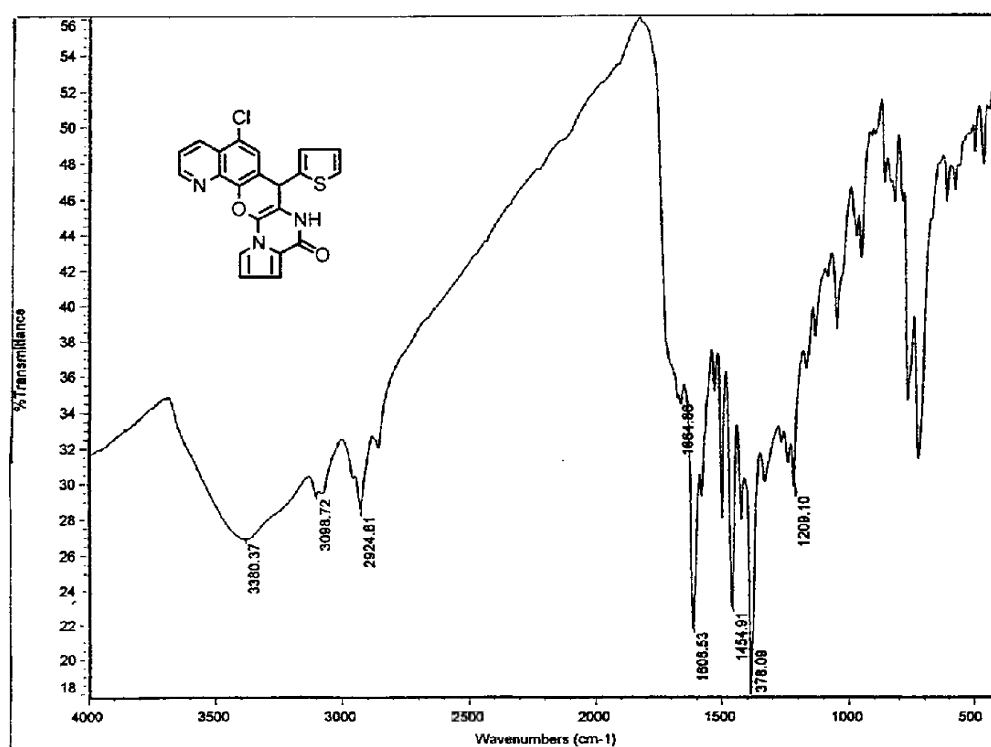


Fig.(116): 5-Chloro-7-thienyl-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**244c**).

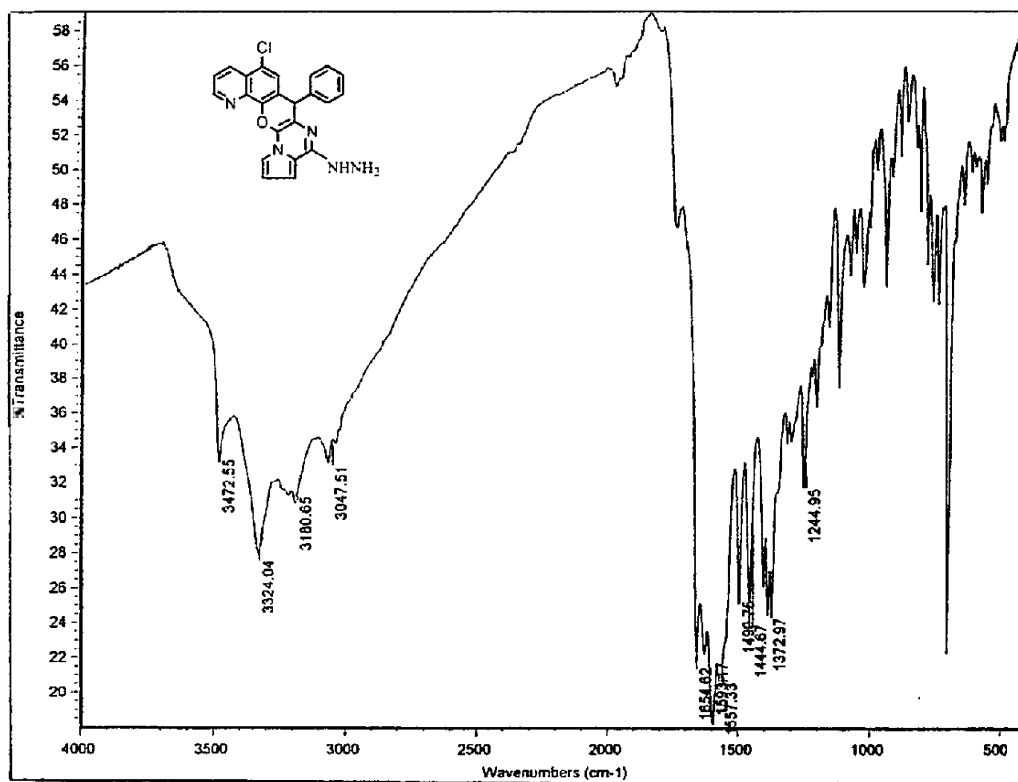
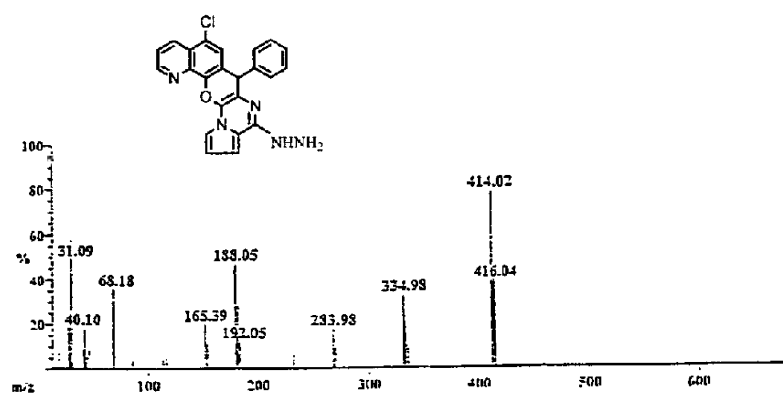


Fig.(117): 5-Chloro-9-hydrazino-7-phenyl-7H-pyrrolo[1",2":1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**246_a**).

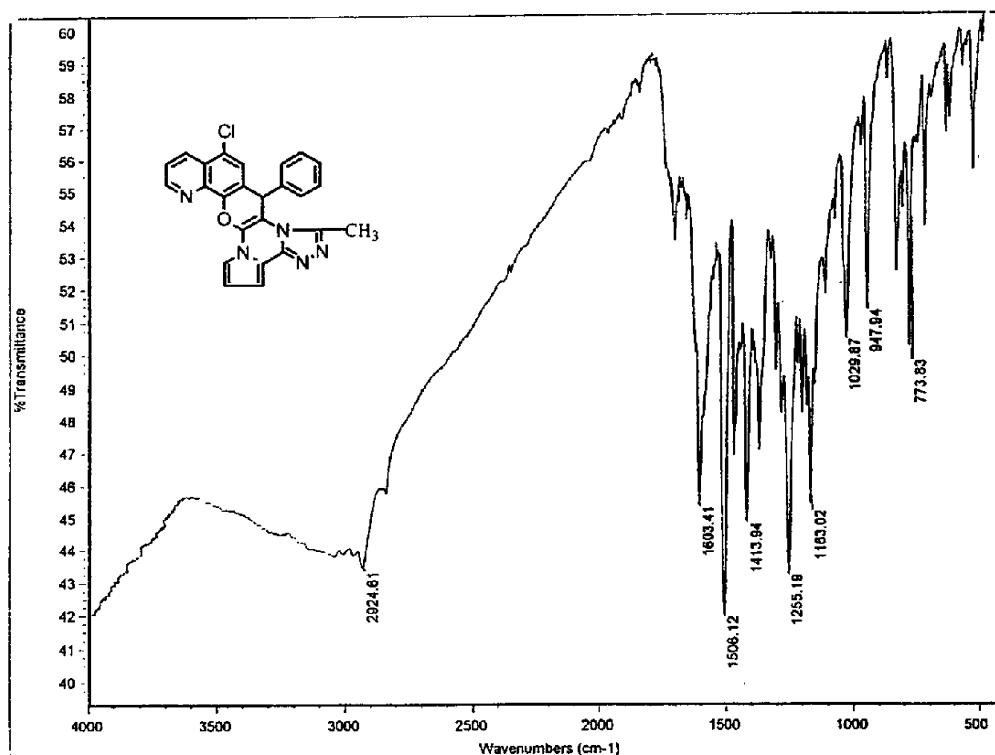


Fig.(118): 5-Chloro-9-methyl-7-phenyl-7H-1,2,4-triazolo[3'',4'':3',4']-pyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**247_a**).

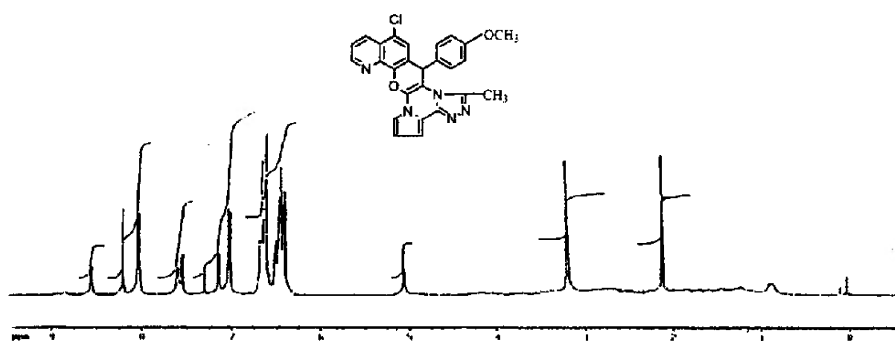


Fig.(119): 5-Chloro-9-methyl-7-(4-methoxy)phenyl-7H-1,2,4-triazolo-[3'',4'':3',4']pyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**247_b**).

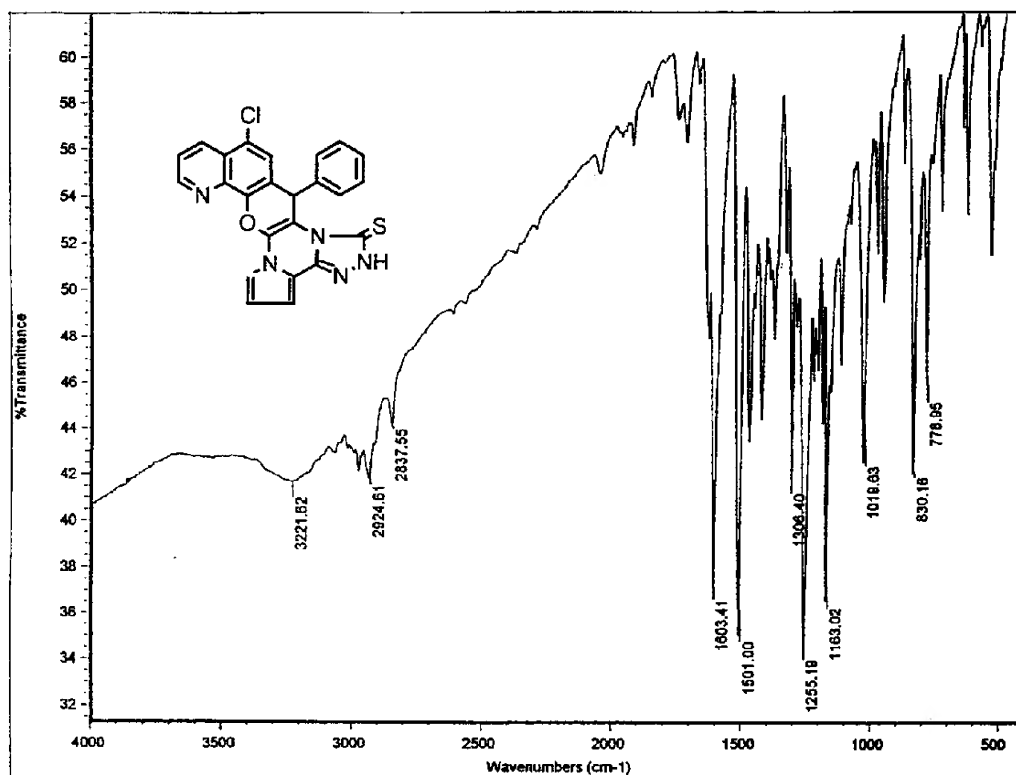
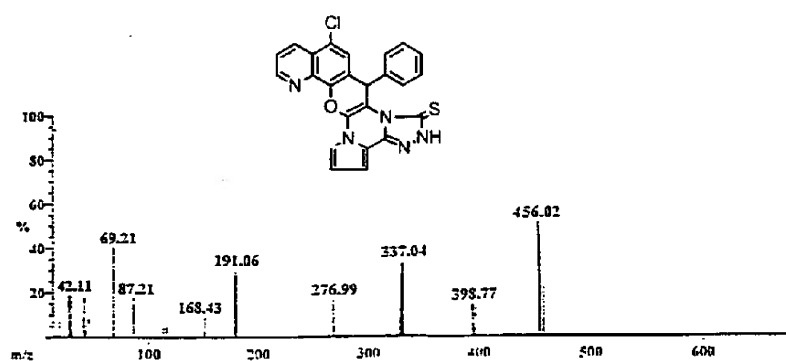


Fig.(120): 5-Chloro-7-phenyl-9-thioxo-7,10-dihydro-1,2,4-triazolo[3'',4'':3',4']-pyrrolo[1'',2'':1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**248_a**).

Arabic Summary

الملخص العربي

تعتبر مركبات البيران و البيريميدين و الكينولين و الاميدازول و التريازول و التريازين و البيروول و الديازين ذات نشاط بيولوجي فعال. فمركبات البيران تستخدم كمضادات للبكتيريا و الفطريات و الأورام و التوتر و الكينولين كمضادات للملاريا و البكتيريا و الفطريات و الربو و القرع و تصلب الشرايين و كمبيدات للأعشاب. و البيريميدين كمضادات للبكتيريا و الفطريات و الفيروسات و السرطان و الشلل الرعاش و كمبيد للأعشاب أيضا. و الاميدازولات لعلاج ضغط الدم المرتفع و الحساسية و داء البول السكري و الأمراض البكتيرية. التريازولات و التريازينات كمضادات للبكتيريا و الفطريات و كمبيدات للحشائش و أنشطة مختلفة أخرى ذات قيمة علاجية. و نتيجة لهذه القيمة العلاجية فإنه من الفائدة عند دمج بعض هذه الحلقات في جزئ واحد الحصول على مركبات جديدة ذات قيمة علاجية.

بناء على ذلك فقد تم اصطناع العديد من المشتقات الحلقية الغير متجانسة الجديدة ثلاثية النواة الملتحمة و المحتوية على نواة البيرانوكينولين مثل بيريميدو بيرانو كينولين- بيريدو بيرانو كينولين- تريازينو بيرانو كينولين- و رباعية النواة الملتحمة و المحتوية على نواة البيرانو كينولين مثل إמידازو بيريميدو بيرانو كينولين- تريازولو تريازينو بيرانو كينولين- بيروولو بيرازينو بيرانو كينولين و خماسية النواة الملتحمة و المحتوية على نواة البيرانو كينولين مثل بيروولو تريازولو بيرازينو بيرانو كينولين.

كما احتوت هذه الرسالة على تقييم لنشاط هذه المركبات ضد بعض أنواع من البكتيريا و الفطريات لمعرفة مدى فعاليتها و قد أوضحت الدراسة أن معظم هذه المركبات لها تأثير واضح و فعال كما هو واضح من الجداول المذكورة في الرسالة.